NOV 8 1957

NOVEMBER 1957
VOL. LII No. 11

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M69

VETERINARY Medicine

Established 1905

features in this issue...

Technical Program

of the

Interprofessional Symposium

on

Leptospirosis

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(Complete Index on Page VIII)

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electrolyte depletion and dehydration
often retard or actually prevent recovery

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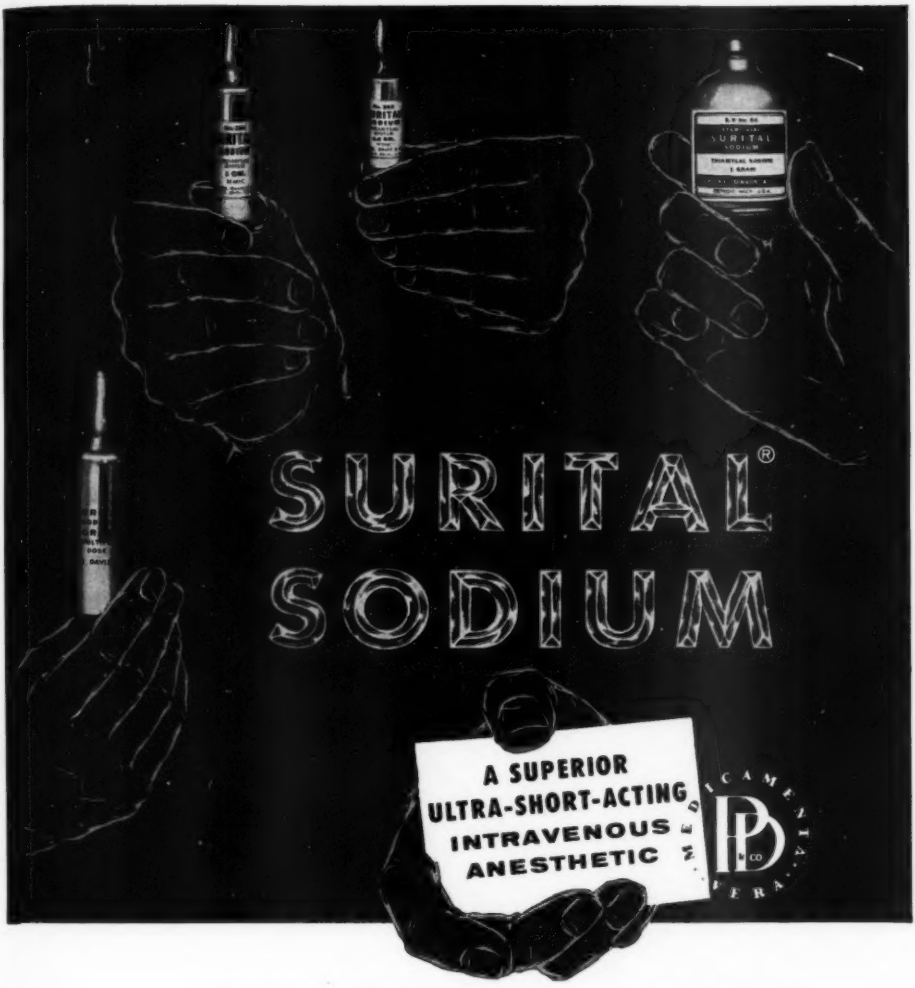

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Department of Veterinary Medicine

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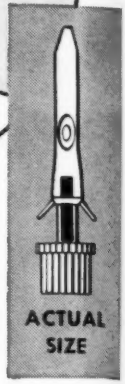

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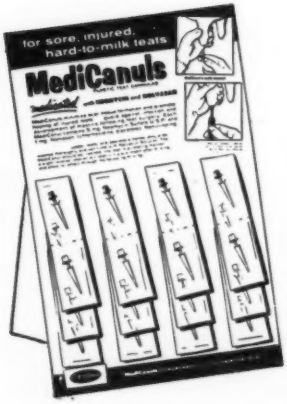

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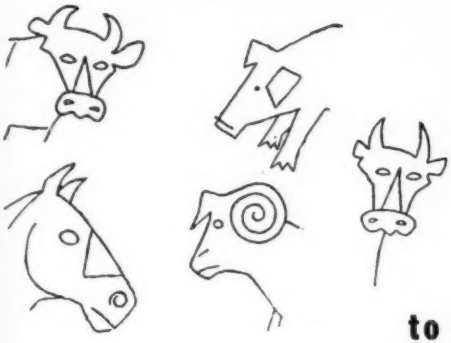

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By

ARNOLD

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PRODUCT	DESCRIPTION	INDICATIONS
DIENESTROGEN	5 mg. Dienestrol/cc. in special oil base. 10 cc. vials.	To promote conception in "shy-breeding" cows.
ESTRADIOGEN	3 mg. Estradiol Dipropionate/cc. in special oil base. 10 cc. vials.	For anestrus, mummified fetus, pyometra, urinary incontinence, enlarged prostate.
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PROGESTERONE	10 mg. Progesterone/cc. in special oil base. 10 cc. vials. 50 mg. Progesterone/cc. in oil with 10% benzyl alcohol. 10 cc. vials.	To prevent habitual and threatened abortion, treat cystic ovaries and nymphomania, delay estrum, stimulate endometrial development and secretions, favor nidation of ovum.
STILBESTROGEN	Diethylstilbestrol fortified with Estradiol Dipropionate in special oil base. No. 4—4 mg. Stilbestrol w/1600 units Estradiol per cc. 60 cc. vials. No. 10—10 mg. Stilbestrol w/4000 units Estradiol per cc., 30 cc. and 60 cc. vials. No. 25—25 mg. Stilbestrol w/10,000 units Estradiol per cc., 10 cc. and 30 cc. vials.	For anestrus, retained placenta, mummified fetus, pyometra, inhibition of lactation, urinary incontinence, vaginitis in spayed bitches.
TESTANDROGEN	Testosterone Propionate/cc; 25 mg. in oil, 10 cc. vials. 50 mg. in oil, with 2% benzyl alcohol, 10 cc. vials. 100 mg. in oil with 10% benzyl alcohol. 10 cc. vials.	For cryptorchidism; hypogenitalism; hypogonadism; impotency; senility; eczema; stimulation of bone formation, fracture repair; osteoporosis; inhibition of lactation; mammary carcinoma.

WRITE FOR COMPLETE CATALOG OF VETERINARY SPECIALTIES

Arnold

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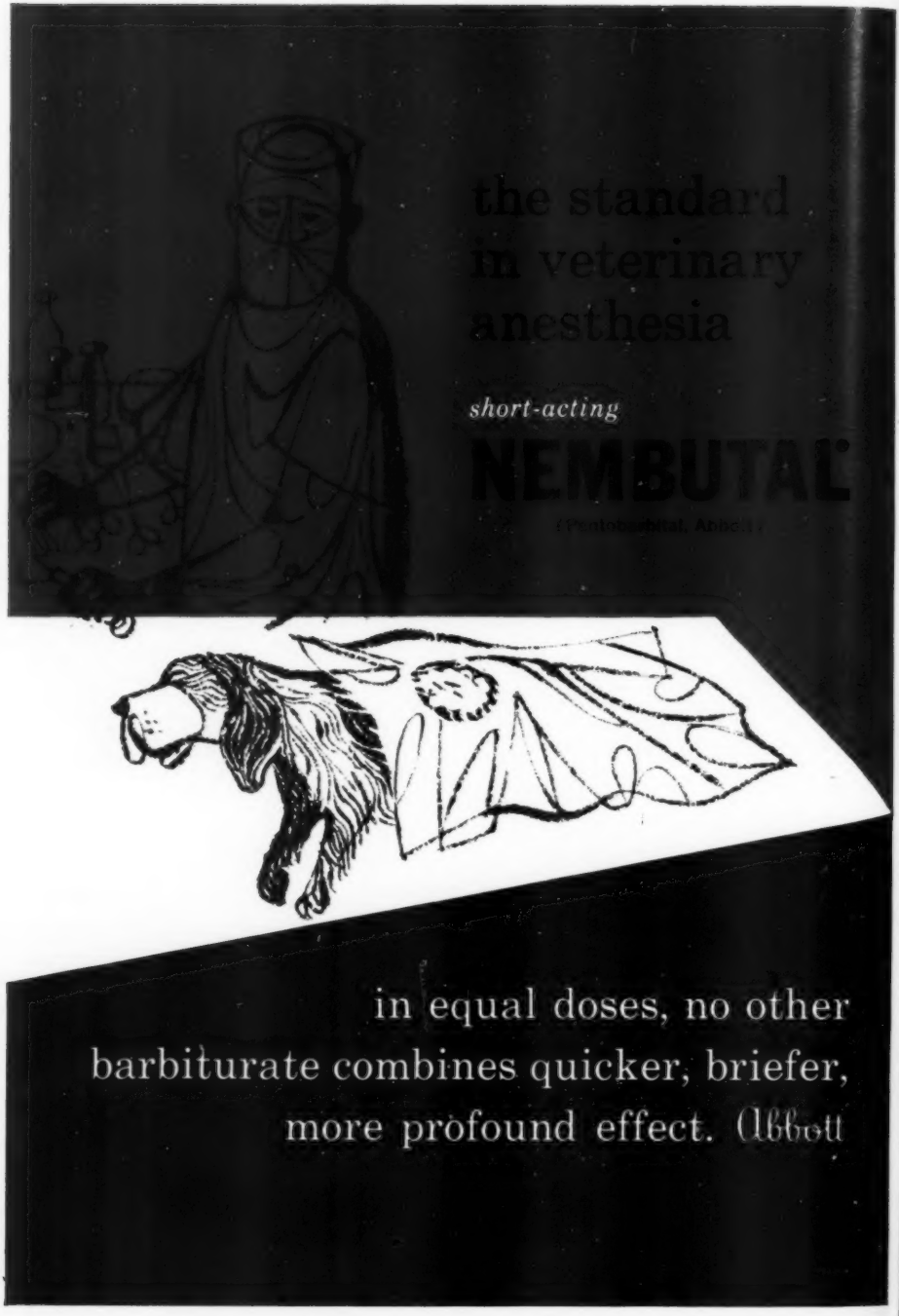
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more profound effect. Abbott

NEWS COMMENT

Recent Losses from Anthrax

A late summer outbreak of anthrax in northeastern Oklahoma and southeastern Kansas caused serious losses to livestock interests. The situation is now completely under control. Few cases have been reported since Sept. 20, 1957.

An extensive vaccination program was started in Oklahoma soon after diagnosis of anthrax was confirmed. Approximately 150,000 animals were vaccinated with a noncapsulated vaccine. No losses were reported in herds that had been vaccinated for at least ten days.

Infection occurred, according to USDA report, in 346 herds. Reported cases approximated 1,200 animals; 880 were cattle. Estimated deaths in the two-state area were as follows: 704 cattle, 64 horses and mules, 140 sheep and goats, and 65 swine; a total of 973 head.

Sex Control in Cattle

Dr. Manual Gordon, geneticist, has been credited with what is described as "apparently the first genuine success in the control of sex that has been reported in the western world."

The general principle involved is based upon electrical properties of sperm cells; those carrying chromosomes which produce females are attracted to positively charged anodes; those which produce males are attracted toward negatively charged cathodes; and the entire process is called electrophoresis.

In trials with rabbit semen, sex of individuals in litters produced was predetermined accurately 70% of the time.

Germ Incubation Vest

Bacteriological field tests can now be facilitated through use of an inoculation vest recently developed by scientists of the Biological Warfare Laboratories, U.S. Army, Fort Detrick, Maryland.

The vest provides for incubation of samples by maintaining them at body temperature from the moment they are collected until returned to the laboratory. The new device eliminates refrigeration and at the same time hastens the growth of clusters of bacteria, the first step in routine tests for identification of microbes.

Poultry Inspection Needed

The Inspection Branch, Poultry Division, Agricultural Marketing Service, USDA, is charged with the responsibility for administration of the recent passed Poultry Inspection Act.

Poultry processors seeking classification as official establishments are creating further demands for trained veterinary inspectors. Positions are opened and appointments will be made on the basis of application submitted. Those interested should inquire at the local office of the Agricultural Marketing Service.

VETERINARY Medicine

Established 1905

Registered in U. S. Patent Office

A Monthly Magazine Devoted to the Promotion of the Art and Science of Veterinary Medicine

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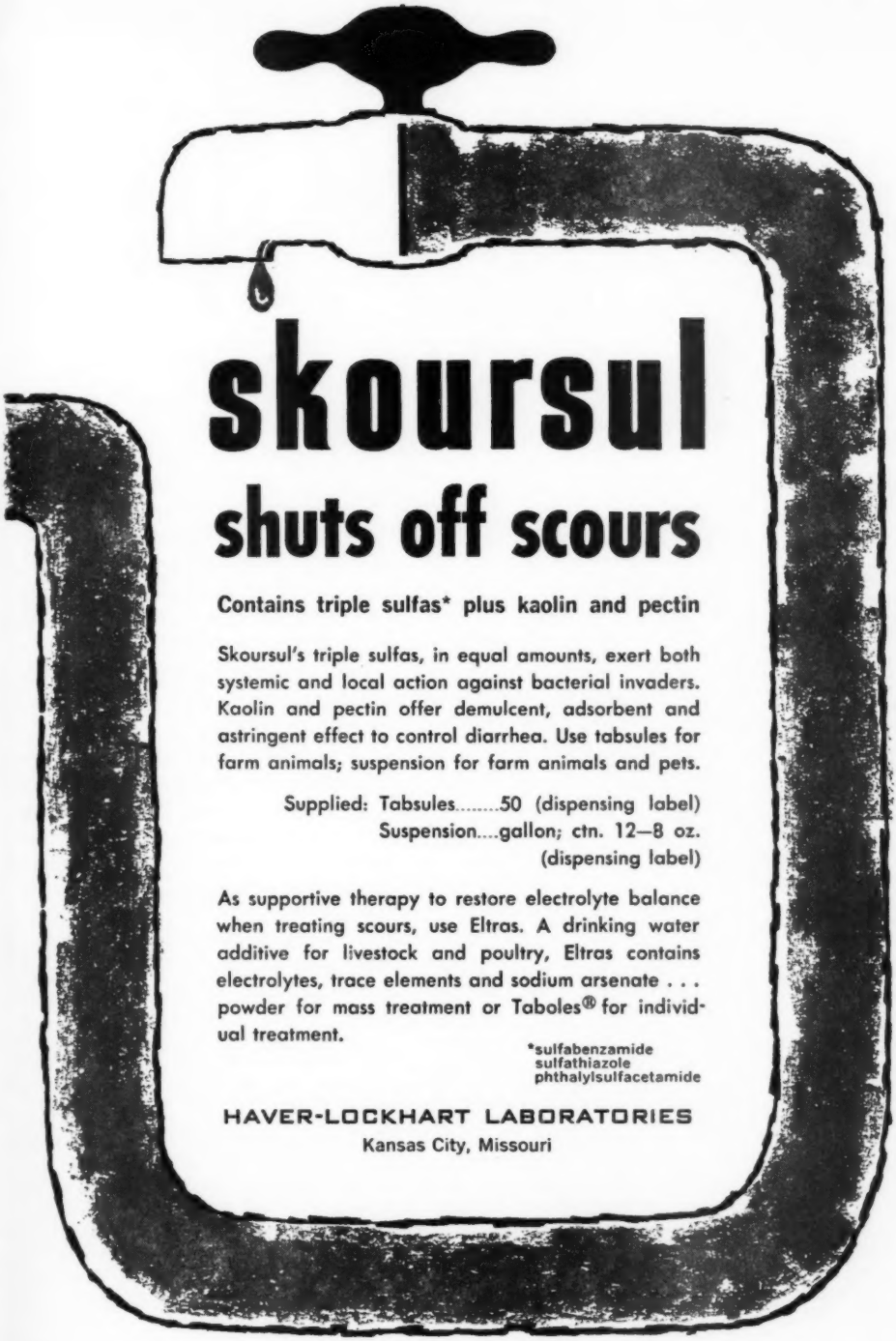

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shuts off scours

Contains triple sulfas* plus kaolin and pectin

Skoursul's triple sulfas, in equal amounts, exert both systemic and local action against bacterial invaders. Kaolin and pectin offer demulcent, adsorbent and astringent effect to control diarrhea. Use tabsules for farm animals; suspension for farm animals and pets.

Supplied: Tabsules.....50 (dispensing label)
Suspension....gallon; ctn. 12—8 oz. (dispensing label)

As supportive therapy to restore electrolyte balance when treating scours, use Eltras. A drinking water additive for livestock and poultry, Eltras contains electrolytes, trace elements and sodium arsenate . . . powder for mass treatment or Taboles® for individual treatment.

*sulfabenzamide
sulfathiazole
phthalylsulfacetamide

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Implanted between the skin and cartilage of a steer's ear, Synovex stimulates higher weight gains at *lower cost per pound of gain.* Feed conversion is improved as much as 20% over controls. Tests prove that Synovex has increased rate-of-gain up to 50% over Stilbestrol with *no downgrading of carcass quality.*

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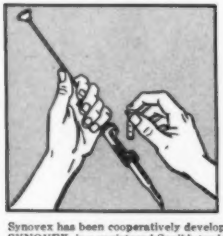
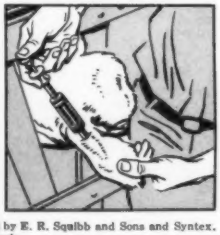
Insert plastic cartridge containing six pellets of Synovex into the chamber of the implanter.



Nick through skin of ear with special scalpel. Insert tip of implanter, press plunger to eject all six pellets of Synovex.



Synovex has been cooperatively developed by E. R. Squibb and Sons and Syntex. SYNOVEX is a registered Squibb trademark.

*R. J. Deans, W. J. Van Arsdell, E. P. Reineke and L. J. Bratzler (Michigan Agricultural Experiment Station): The Effect of Progesterone-Estradiol Implants and Stilbestrol Feeding on Feed Lot Performance and Carcass Characteristics of Steers. Journ. Animal Sci. 15:1020, 1956.

SQUIBB QUALITY

5¢ PER LB. OF GAIN

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SYNOVEX IMPLANTS MAKE FEED STORAGE EASIER. Selected animals can be treated without the need for separate feeding programs or special feed storage facilities. There is no danger of breeding stock accidentally receiving hormones in their feed. Because Synovex continues to be absorbed at a pre-calculated rate for the entire finishing period, implanted steers receive a controlled hormone dosage every day—a degree of control not possible when hormones are mixed with feed.

SYNOVEX IS RECOMMENDED FOR STEERS WEIGHING FROM 400 TO 1,000 LBS. ONE IMPLANT LASTS A FULL 150 DAYS.

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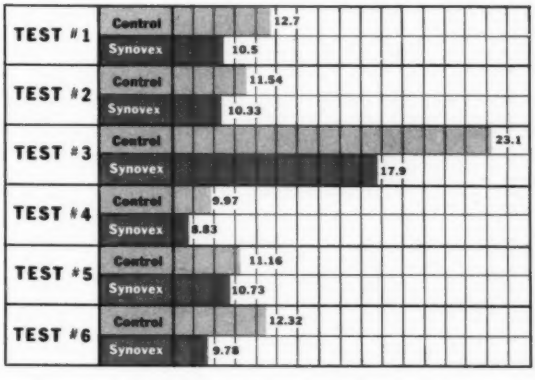
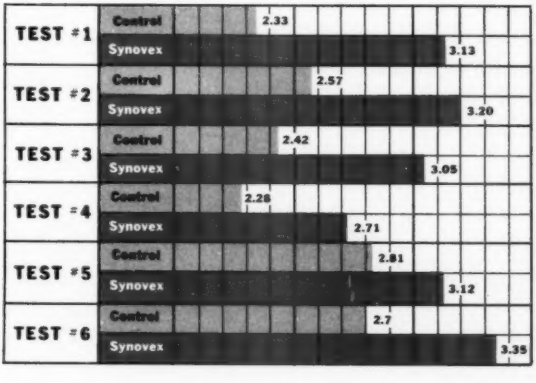
Lbs. of feed per lb. of gain



Gain per head per day



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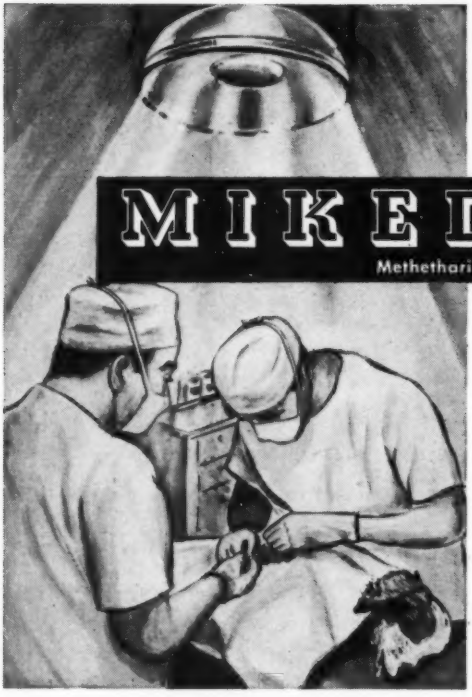

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THE BARBITURATE ANTAGONIST OF CHOICE

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MIKEDIMIDE *is indicated*

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SUPPLIED: Each bolus contains 0.12 grams of FURACIN and 12 grams urea. Bottle of 25.

DOSE: Two boluses inserted into the recently pregnant horn. One bolus may be placed in the non-pregnant horn.

*Jones, S. V.; Belloff, G. B., and Roberts, H. D. B.: Vet. Med. 51:413 (Sept.) 1956.

For vaginal infections, including those caused by Vibrio fetus, that may prevent conception, or cause abortion, dispense: FURACIN Suppositories Veterinary, large. Box of 12.

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new specific treatment for calf scours

Developed specifically for the control of calf scours, new ENTEFUR provides rapid, effective and safe treatment. ENTEFUR drastically cuts mortality.[1,2] In one study, 60 of 63 ENTEFUR-treated calves survived, whereas in the control group only 3 of 24 calves lived.[2] "ENTEFUR treatment appeared the only factor modifying significantly the course and outcome of the disease."[2]

ENTEFUR contains the new nitrofuran, Furamazone® (brand of nifuraldezone) for rapid wide-spectrum bactericidal action against gram-positive and gram-negative enteric bacteria. ENTEFUR also contains bismuth subsalicylate for its mildly astringent, antidiarrheal action.

ENTEFUR BOLUS VETERINARY, small, contains: Furamazone 1 Gm., bismuth subsalicylate 0.26 Gm. Dosage: 1 bolus twice a day for 2 days. Supplied: Box of 24 (6 envelopes of 4 boluses each).

REFERENCES: 1. Bull, W. S.: N. Amer. Vet., in press. 2. Henry, R. T., and Blackburn, E. G.: Vet. Med., in press.

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Combats scours, infections, vitamin deficiencies and shipping fever. An excellent nutritional conditioner that enables pigs to gain weight faster by stimulating feed intake.

ADMIT ONE — **RESERVED** — ADMIT ONE

Treats chronic respiratory disease, blue comb and nutritional deficiencies. Stimulates feed intake, resulting in rapid weight gains, and increases egg production.

ADMIT ONE — **RESERVED** — ADMIT ONE

Vistrepcin has proved to be an outstanding treatment for bacterial calf scours . . . controlling the problem within 12 to 72 hours. Is an aid to rapid weight gains, smoother coats, preventing shipping fever and stops coughing after only a few days.

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Effectively combats bacterial diarrhea, nutritional vitamin deficiencies and improves appetites, thereby improving the overall condition of the animal.

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Calcium pantothenate	600.0 mgs.
Niacin	1400.0 mgs.
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Vitamin A (Palmitate oil)	100,000 U.S.P. Units
Vitamin D_3 (In an inert base)	100,000 I.S. Units

PACKED IN 4oz, 1 pound 5 pound and 25 Pound sizes

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decisive, short-term therapy of diarrheas in calves and dogs

VARITON compound

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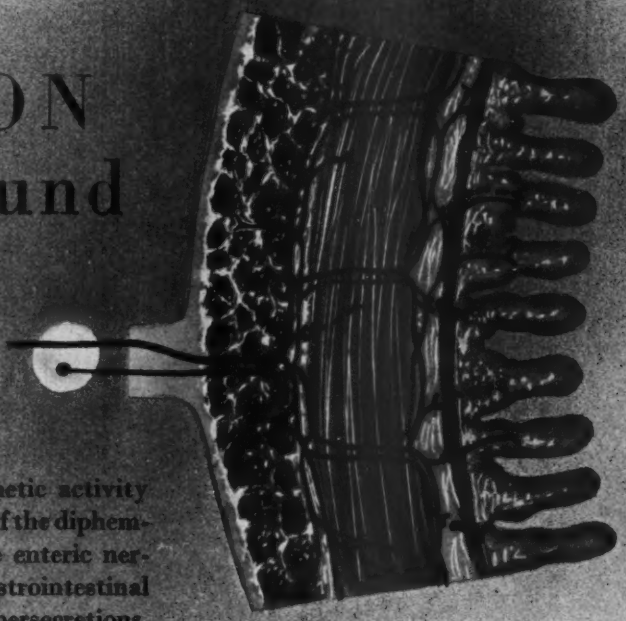

regulates propulsive phase

Blockage of parasympathetic activity by anticholinergic action of the diphemanil methylsulfate on the enteric nervous system lessens gastrointestinal motility and inhibits hypersecretions. These factors contribute directly to the physiological control of diarrheas.

combats enteric infections

Bacteriostatic action of the sulfonamide, phthalylsulfacetamide, attacks infection at the site of enteric infections and on mucosal surfaces. When diarrheas are complicated by systemic infection, appropriate antibiotic-sulfonamide therapy also is indicated.

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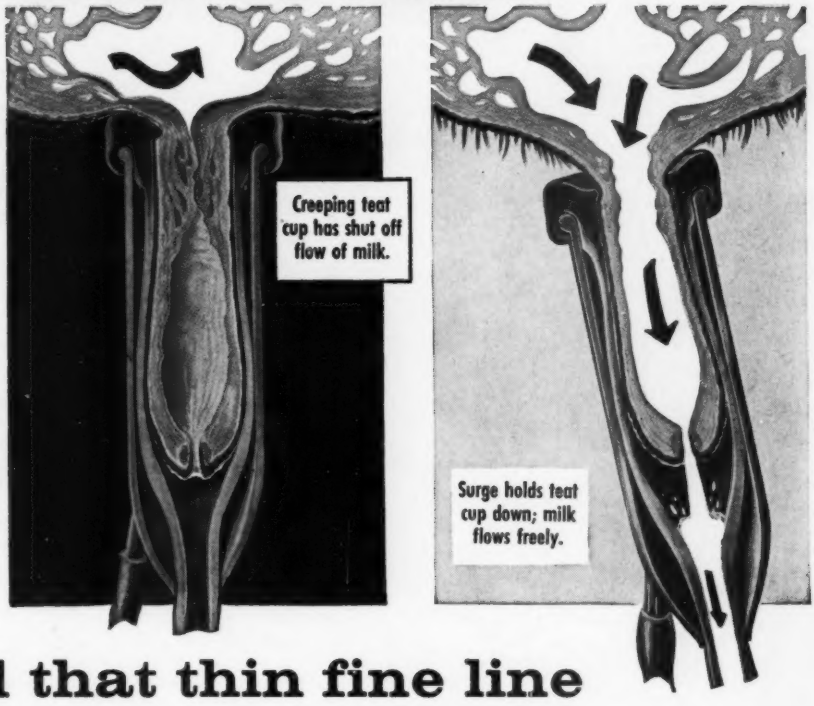

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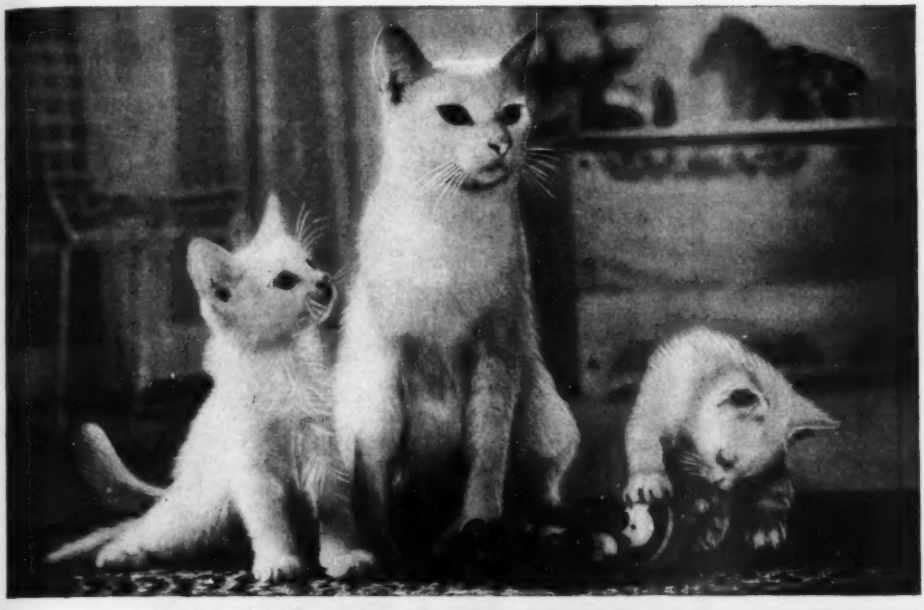

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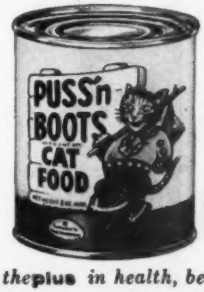

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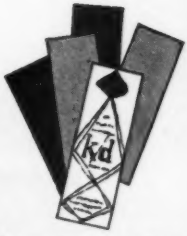

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Interprofessional Symposium on Leptospirosis

In this issue of VETERINARY MEDICINE is reproduced, insofar as practical, the entire program presented as the Interprofessional Symposium on Leptospirosis, which convened at Kansas City, Kansas on April 25, 1957.

World-wide and apparently increasing morbidity due to leptospirosis, in both man and animals, has aroused considerable interest and concern in this disease. The faculty of the Department of Postgraduate Medical Study, University of Kansas School of Medicine, selected leptospirosis for exhaustive discussion because of some peculiar features and variability of the disease that complicate the clinical syndrome in man. Veterinary authorities were consulted in developing the symposium because of basic contributions made in the field of veterinary medicine and also because of the close relationship and transmissibility of leptospirosis between animals and man.

Cooperative Effort

This interprofessional symposium, the first undertaken by cooperating groups in Kansas City was considered a most successful venture; one that has set a pattern for similar cooperative efforts to define current concepts of other zoonoses. The Symposium was presented by the University of Kansas School of Medicine, Kansas City Veterinary Medical Association, and the Department of Health, Education and Welfare, U.S. Public Health Service, in cooperation with the Jackson County Medical Society, the Kansas Medical Society, the Kansas State Board of Health, the Kansas Veterinary Medical Association, and the Missouri Veterinary Medical Association. Sessions were held in the modern Battenfield Auditorium at the Kansas Medical Center. Guest faculty included physicians, veterinarians, public health personnel, and scientists who have studied the disease from various aspects, and who are recognized as international authorities in their respective fields. A total of 350 physicians, veterinarians, and laboratory technologists registered for the one-day symposium. The Armed Services Institute of Pathology and the Veterinary Corps, U.S. Army, presented an educational exhibit featuring leptospirosis which received favorable reception.

Newly Recognized Syndrome

Leptospirosis is not a new disease. It may be referred to as a newly recognized syndrome in the United States. It has only been during the past five years that research workers and veterinarians have been making diagnosis of this infectious disease in livestock with regularity. Yet today, it is estimated that leptospirosis causes a $100,000,000. loss among domestic animals annually in the United States. Thousands of cattle and hogs are involved each year. Economic and veterinary importance of the disease has been grossly underestimated, at least in this country. Some authorities believe the figures quoted do not adequately reflect total loss to growers of food animals.

Public Health Significance

Likewise, it has been pointed out that too little is known about the true public health significance of the leptospiroses. Clinical syndrome is reported to be extremely variable causing difficulties in diagnosis and confusion with a number of other anomalies. It has been pointed out that, on a world basis, 34 distinct pathogenic serotypes of Leptospira have been identified since Weil first described the disease in man in 1886. No less than eight serotypes are of public health and veterinary significance in the United States.

Publication of the Program

Material presented was received enthusiastically. Many of those in attendence inquired about the availability of papers for reading and reference. The editors believe that the discussions as a group reflected most advanced thinking and outlined the latest concepts of this condition. For these reasons permission was requested, and subsequently granted, for publication of the entire program in a single issue of VETERINARY MEDICINE. This has been accomplished this month by deleting regularly scheduled departments and other editorial material. Standard features and departments will reappear in future issues.

Panel Discussion

Closing feature of the all-day session was a panel discussion at which all faculty participated. Lt. Col. William S. Gochenous Jr., V.C., U.S. Army, served as moderator.

In answer to a question concerning possible sterility in cattle following infection, Dr. H. S. Bryan stated that experience in Illinois indicated that herds were affected differently, possibly in relation to severity of the herd outbreak or period of gestation in individual cows. Dr. Charles J. York reported that in

two herds under his observation, invasion by leptospirosis was apparently responsible for an excessive abortion rate, yet during the following two-year period conception rate was normal.

Dr. Herbert G. Stoenner replied to query concerning anthropod vectors that certain ticks had been experimentally infected with various serotypes of Leptospira and that they were able to transmit the disease to experimental animals. He added that he did not believe that anthropod vectors played any significant role in dissemination.

The Chairman answered a question concerning the ability of leptospiral organism to infect man through the unbroken skin by citing immersion experiments that allegedly establish the ability of leptospires to penetrate maserated or soaked human skin. From a practical standpoint, intact, unbroken human skin is probably a figment of imagination in person who work barefooted in rice fields or other place where water may be contaminated by rodents. Carefully controlled studies have shown that a small number, perhaps even a single leptospire, is capable of gaining entrance through minute abrasions and establishing infection.

It was also brought out that no reports of leptospiral infection in man is produced by inhalation or ingestion in which the possibility did not also include exposure by contact with mucous membranes or skin abrasions; roots of infection that are well established.

In response to the question of a national control or eradication program directed toward the disease in livestock, it appeared to be the consensus of the panel that such a step must await standardization of serological procedures.

In a study of 300 serum samples from cats, 5% were shown to be positive by the agglutination-lysis test.

Leptospirosis in a dairy herd is not, as some believe, a continuing problem but a self-limiting one. In most cases the disease has run its course within a year after which the contagious potential in the herd no longer exists. Serological positives does not mean such animals are shedders of viable organisms. Many cows remain serologically positive for years, whereas most cases cease to be urinary shedders after three or four months.

Clorination of water as is practiced routinely at public swimming pools is considered effective control assuring safety of swimmers in the event of accidental contamination.

The meeting was closed on the optimistic note that an alert medical and veterinary profession have developed new information rapidly of tremendous value in the control of leptospiroses in both man and animals. It is expected that further facts will be forthcoming from intensive research now underway in many parts of the world.

Some of the speakers at the Interprofessional Symposium on Leptospirosis are: Lt. Col. William S. Gochenour Jr., at rostrum, and l. to r. Dr. Herbert G. Stoenner, Dr. M. J. Twiehaus, Dr. Harold S. Bryan, Lt. Col. Leslie C. Murphy, Dr. Charles J. York, Dr. J. E. Mosier, Dr. John T. Logue, Dr. Joe L. Stockard, and Dr. James H. Steele.

Leptospirosis As A World Problem†

JAMES H. STEELE,* D.V.M., M.P.H., MILDRED M. GALTON,* Sc.M., and R. W. MENGES,* D.V.M., M.P.H., Atlanta, Georgia

DURING the past half-century, extensive studies have shown that leptospirosis occurs in man and animals in all parts of the civilized world. For many years, it was thought to be a rare disease and progress in the accumulation of knowledge regarding the clinical manifestations, epidemiology, public health importance, and distribution has been slow. In 1886, Weil[1] described several human cases of leptospirosis although he had no knowledge of the causative agent. The classic disease has since been known as Weil's disease. Nearly 20 years later, leptospires were seen first in New Orleans by Stimson in sections of kidney from a patient believed to have died of yellow fever.

Early History

Pathogenic leptospires were isolated first from cases of Weil's disease in Japan by Inado and Ido in 1915[2] and independently in Germany by Uhlenhuth and Fromme[4] in the same year. These investigators followed Stimson's earlier designation and placed the organisms in the genus Spirochaeta. It was not until 1917, that the genus Leptospira was established by Noguchi.[5] The Japanese workers found that the rat (*Rattus norvegicus*) is a carrier of *Leptospira icterohemorrhagiae*. About the same time, these investigators isolated *L. hebdomadis* and *L. autumnalis* from cases of mild febrile illness. This stimulated Dutch workers to study methods for classifying leptospires. It soon became apparent that differentiation was possible only by the use of serological procedures. As other antigenically distinct serotypes were isolated in Europe, Asia, Africa, Australia, and Indonesia technics for serologic identification were developed and refined. Finally, in 1954, Wolff and Broom[6] published a suggested classification system based on antigenic analysis which included 34 leptospiral serotypes isolated from man and/or animals. In the comparatively short period since this report, at least 25 additional serotypes have been described from Malaya by Alexander,[7] from Australia by Smith[8] and the Belgian Congo by Van Riel.[9] The value of differentiation of strains of pathogenic leptospires is obvious if further knowledge is gained regarding the epidemiology, ecology, public health importance, and prevalence of these infections. That leptospirosis is now recognized as a disease of increasing world-wide significance may be attributed to the following factors:

1. An increasing awareness of physicians and veterinarians to the possibility of infection.
2. A broader concept of the clinical manifestations to be expected.
3. A better knowledge of the widespread distribution of leptospires in animals.
4. And more recently, the increasing demand for leptospiral diagnostic laboratory services.

†Presented at the Interprofessional Symposium on Leptospirosis. Postgraduate Medical Study, University of Kansas Medical Center, Kansas City, Kansas, April 25, 1957.

*Communicable Disease Center, Public Health Service, Bureau of State Services, U. S. Department of Health, Education and Welfare.

TABLE 1. Leptospirae in the United States

Serotype	Original isolation	Known host	Occurrence			
			Man	Dogs	Cattle	Swine
L. icterohemorrhagiae	Japan Germany	rat	common	occasional	?	?
L. canicola	Netherlands	dog	occasional	common	rare	rare
L. pomona	Australia	swine, skunk racoon, wildcat	occasional	rare	common	common
L. autumnalis	Japan	opossum racoon	rare	?	?	?
L. ballum	Denmark	mice, gray fox, opossum, wildcat, rat, racoon, striped skunk	?	?	?	?
L. grippotyphosa	Russia	racoon	rare*	?	?	?
L. bataviae	Indonesia	?	rare*	?	?	?
L. sejroe	Denmark	?	?	?	sporadic	?
L. australis A	Australia	racoon	?	?	?	?
*L. bakeri***	United States	opossum	?	?	?	?

*Serological evidence only; **_mitis-hyos_ serogroup.

Foreign Distribution of Leptospires

In considering the extent of the distribution of individual serotypes, Broom[10] speculates about the means by which a single type spreads across the world. He is of the opinion that the westward spread of *L. icterohemorrhagiae* in Eurasia may have been a result of the migration of *R. norvegicus*, the primary host of this serotype. Upon reaching the seaports, rats were carried in ships to many countries. It is interesting, however, that certain areas of the world such as the Anglo-Egyptian Sudan, and South Africa, appear to be free from leptospirosis even though it is present in neighboring countries. For example, in the Sudan, Kirk (1938)[11] examined 259 rats of which 42% were *R. norvegicus* and failed to find leptospires. In South Africa, Buchanan[12] found no evidence of leptospiral infection in rats and other rodents nor did he find leptopiral antibodies in the serums from 200 patients with "jaundice." By contrast Van Riel[9] has reported 45 laboratory confirmed cases of leptospirosis among workers in tin mines of the Belgian Congo. At least five serotypes were found including members of the *L. icterohemorrhagiae*, *L. hebdomadia*, and *L. hyos* serogroups, *L. bataviae* and *L. grippotyphosa*. It is interesting that the majority of these cases were anicteric. In addition, Van Riel, has found evidence of leptospiral infections in dogs (1946),[13] swine[14] and cattle[15] in the Belgian Congo. One wonders whether the apparent absence of leptospirosis in other areas of Africa is due to particular epidemiologic, ecologic and geographic factors or whether more intensive studies would reveal evidence of the disease. No doubt, the reported prevalence of leptospirosis in different countries is influenced not only by the extent of the problem in man and animals but also by availability of laboratory diagnostic services and interested investigators.

During the initial investigations in Israel by Bernkopf and associates[16] leptospirosis due to *L.grippotyphosa* occurred in cattle and human beings who had close contact with cattle.

Subsequently the isolation of *L. grippotyphosa* from voles and the increase in human cases with no cattle contacts indicated that voles are the main reservoir.[17] More recently, severe outbreaks of *L. canicola* infection in cattle have been observed in Israel and a relatively large number of human cases occurred. Pigs and jackals as well as dogs serve as reservoirs of *L. canicola*. Van der Hoeden[18] believes that their recent observations indicate consideration of canicola fever as an occupational disease.

Several epidemics due to *L. canicola* have been reported in Japan in recent years.[19] These outbreaks were thought to be waterborne infections, presumably water contaminated by dogs.

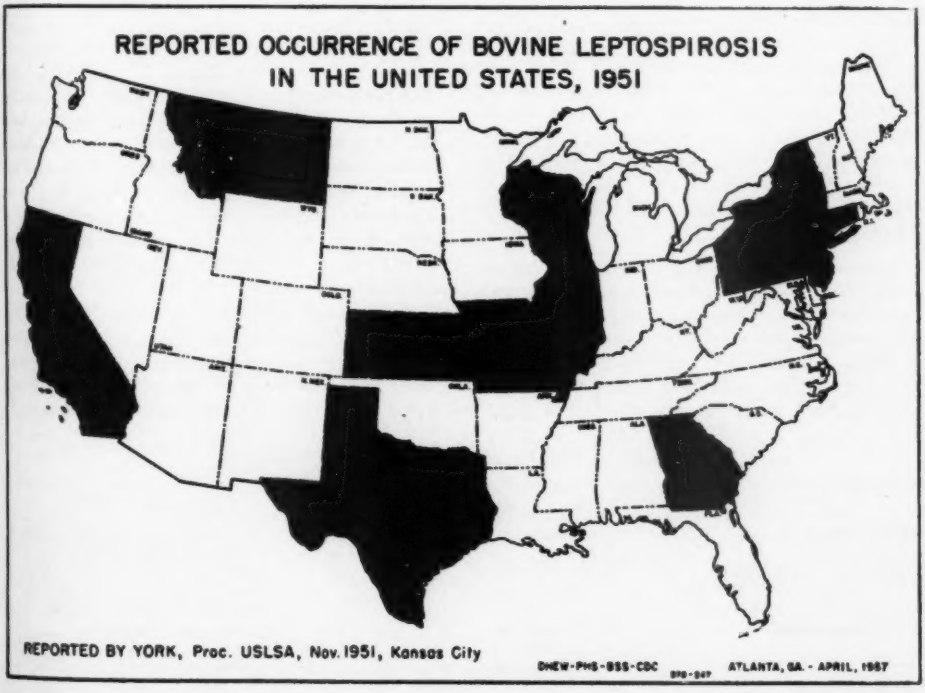
Leptospirosis reported first in Germany in 1915, has continued to occur. A recent report from the Institute of Hygiene in Frankfort[20,21]

indicates that human infections are caused primarily by *L. icterohemorrhagiae* and *L. canicola*, although *L. sejroe*, *L. saxkoebing* and *L. grippotyphosa* infections are found occasionally. The disease is quite prevalent in dogs with approximately 75% of the infections due to *L. canicola*, 15% to *L. icterohemorrhagiae* and the remaining due to other types. A high percentage of rats and mice have been found to carry leptospires particularly those caught around sewage or garbage disposal areas. Human infections occur largely as a result of contact with water, swimming or accidental immersion, believed to be contaminated by infected dogs, rats, or mice.

In the Netherlands reported cases of leptospirosis have been shown by Wolff[22] to decrease gradually from 114 in 1934 to 23 in 1951. During this period the average number of cases per year diagnosed as Weil's disease ranged from 30 to 15. As in Germany, human infection due to *L. canicola* rates second only to infection caused by *L. icterohemorrhagiae*. During the war years (1940-1945) infections due to water accidents increased. Wolff attributes this to greater rat infestation of premises and canals during the war and an increase in the number of water accidents (persons falling in canals) due to the blackout. *L. canicola* was isolated first from a dog that died of the disease in 1931 in Utrecht.[23]

Much of our knowledge and current concepts of leptospirosis have been gained through the intensive investigations of Dutch workers in Indonesia initiated by Schuffner in 1918 and continued until the outbreak of World War II. Of the 34 presently recognized leptospiral serotypes, 18 were initially described by Collier[24] from Indonesia. According to Walch-Sorgdrager *et al.*,[25] 1,531 cases were diagnosed clinically between 1932 and 1938 in East Coast Sumatra of which 426 yielded leptospires on culture. These cases occurred primarily among laborers on rubber plantations and were due to *L. pyrogenes*. This type was found also in field rats (*Rattus brevicandatus*). However, leptospirosis appears to be a problem here in both the rural and urban population. In addition to prevalent rodent infection with a variety of types, infections in dogs were found frequently with *L. hebdomadis*, *L. bataviae* and rarely with *L. pomona*. The isolation of *L. bataviae* from

FIGURE 1.


REPORTED OCCURRENCE OF BOVINE LEPTOSPIROSIS
IN THE UNITED STATES, 1951
REPORTED BY YORK, Proc. USLSA, Nov. 1951, Kansas City
DHEW-PHS-BSS-CDC
ATLANTA, GA. - APRIL, 1957

eight and *L. javanica* from six cats by Esseveld and Collier[26] is most interesting. Human infections in Indonesia are believed in many instances to be contracted through direct contact with infected cats and dogs.

Other areas of southeast Asia have been found to be an important focus of epidemic and endemic leptospirosis. The early studies of Fletcher[27] in Malaya established the presence of *L. icterohemorrhagiae, L. pyrogenes,* and *L. autumnalis* in man. In addition he isolated strains related to *L. autumnalis* from rural black rats and from a dog. Subsequent to these studies, there was a lapse of 25 years before further work was done in Malaya. Interest was renewed with the appearance of a high incidence of clinical disease in the British troops patroling in the jungle areas.[28] During the next three years, intensive studies in Malaya were undertaken by members of the Walter Reed Army Institute of Research (WRAIR) and British workers. A serologic survey reported by Wisseman *et al.*[29] indicated that leptospirosis was prevalent in about one-fourth of the human population, one-third of the domestic animals, and one-sixth of the wild rodents. There seemed to be no difference in the incidence of disease in man from urban, rural, or jungle areas. Particularly high incidence of antibodies appeared in horses, oxen, pigs, and dogs. A multiplicity of leptospiral serotypes, including many new types, have been isolated from both man and rodents. A limited study in British North Borneo indicated that leptospirosis is highly prevalent in the indigenous population and in rodents. These authors also report the isolation of several serotypes from wild rodents in Thailand and Korea.

Leptospirosis was not diagnosed in Australia until 1934 when an outbreak occurred among cane-field workers due to *L. australis A*. Shortly afterwards *L. pomona*[30] was isolated first from a dairy farmer near the town of Pomona and later from swine and cattle. Extensive investigations have shown since that leptospirosis is endemic in the cane growing regions of North Queensland and the dairy and pig raising districts of South Queensland, New South Wales, and Western Australia. The Australian investigators[31] have classified the leptospiroses according to clinical type, infecting serotype, and animal reservoir.

The disease occurs largely among occupational groups with the highest incidence in cane-field and other outdoor workers, dairy and pig farmers, butchers, and abattoir workers.

While most *L. australis A* infections were associated with cane-fields, infections among cane-field workers have included at least ten other types.[32]

It is interesting that many of the "Australian leptospiroses" have been reported also in Switzerland. A fever, for many years known as "Swineherd's disease," was shown by Gsell in 1944[33] to be due to *L. pomona*. Similarly, *L. mitis* was found in Swiss patients who had contact with pigs[34] and *L. australis A* infections were reported in 11 patients who probably contracted the disease in mud contaminated by shrewmice.

Similarly recent studies in Czechoslovakia[35,36,37] revealed that *L. pomona* and *L. mitis* are highly prevalent in swine and in butchers. These two types and 30 other serotypes including *L. canicola, L. sejroe* and *L. ballum* were isolated from 50 (11%) of 460 healthy pigs. In addition *L. australis A* and *L. grippotyphosa* has been found in butchers. During further investigations of leptospiral foci in Czechoslovakia, 2,500 free living animals mostly rodents were examined. Sixty-four leptospiral strains including eight serotypes were isolated from 17 different species of mice and from the hedgehog. Both the yellow throated mouse and the hedgehog were found to be carriers of *L. australis A*.

In nearby Hungary, Kemenes[38] has reported the isolation of 51 leptospiral strains from man, domestic animals, and rodents. The predominant type was *L. pomona* from pigs, cattle, horses, and man. *L. pomona* in-

TABLE 2. Animal Reservoirs of Australian Leptospiroses

Clinical Type	Serological Type	Animal Reservoirs
Classic Weil's disease	*L. icterohemorrhagiae*	Important rats (*R. norvegicus, R. rattus*), dogs
Cane-field leptospiroses	*L. australis A*	Native rat (*R. constas*)
	L. australis B	Imported rat (*R. rattus*) Bandicoot (*Isoodon sp.*)
Mild leptospiroses	*L. pomona*	Cattle, pigs, dogs
	L. mitis	

From Johnson[31], 1950.

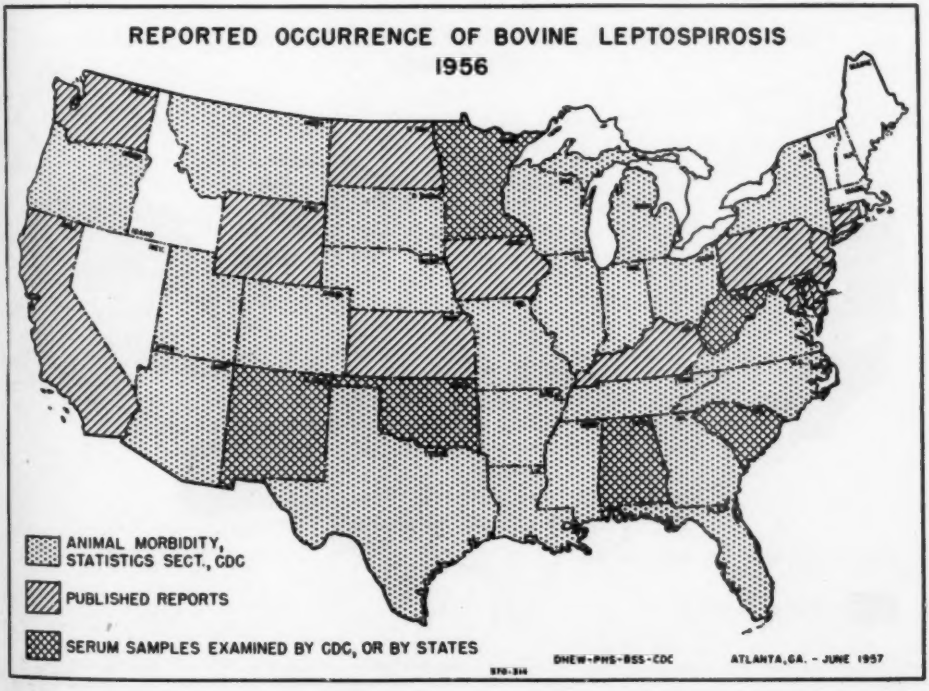
fections in man and adult animals were mild, in calves severe and sometimes fatal infections were observed. *L. mitis* usually occurred simultaneously with *L. pomona*. The author considers the *L. grippotyphosa* and *L. pomona* strains isolated in Hungary identical with strains described in Russia, as *L. icteroanaemiae* types I and II respectively. The isolation of *L. sejroe* from man, rats, and a horse are reported. It is interesting that *L. sejroe* infection in a dog has been reported from Yugolavia.[39]

Recent studies in New Zealand by Kirschner[40] have indicated widespread leptospiral infections in man and domestic animals. Kirschner[40] has reported that 67% of 130 human cases occurred among dairy farmers and the remainder were pig breeders or abattoir workers. Evidence of infection with *L. icterohemorrhagiae, L. canicola, L. pomona* and *L. mitis* has been obtained.

A further example of the widespread distribution of leptospirosis among certain occupational groups in different countries has been demonstrated among rice-field workers in Italy[41] and Spain.[42] In Italy some 600,000 persons are engaged in work in the rice-fields. Babudieri has found that more than 80% of the individuals who have worked in the rice-fields for 20 years or more show leptospiral antibodies. Although infections are primarily with *L. icterohemorrhagiae* and *L. bataviae* at least eight other serotypes have been found. In one instance, an outbreak of *L. pomona* infection occurred involving 60 persons in one rice-field.[43] This type was also isolated from a rat. Rodents appear to be the principle source of infections in the rice-fields. Babudieri has observed that *L. pomona* infections contracted by contact with swine in Italy usually are characterized by meningeal symptoms while those in rice-field workers usually are subclinical. In this connection it is interesting that *L. sejroe* and *L. saxkoebing* infections among rice-field workers in Italy are severe and sometimes fatal. Such infections in Denmark where the strains were initially isolated are usually mild. In Spain, rice-field fevers are caused primarily by *L. icterohemorrhagiae* and *L. ballum*.

The Danish investigations on leptospirosis commenced in 1934[44] and for the next 20 years were focused on infections in humans, dogs, and rodents. Since 1954[45] studies were broadened to include cattle and antibodies against

FIGURE 2.



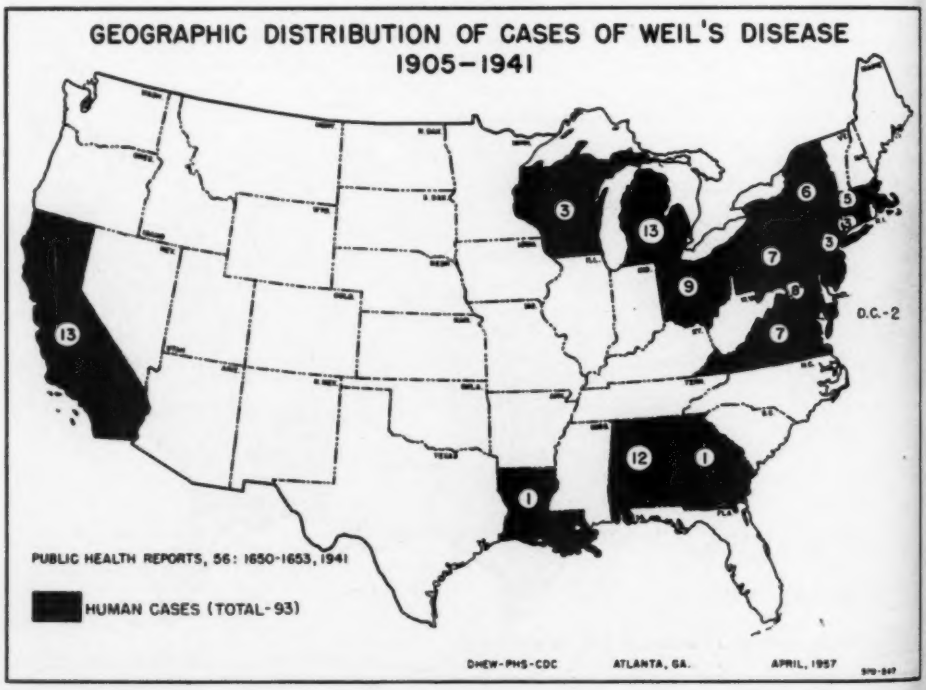
one or more of the nine serotypes known to exist in Denmark were found in about 8% of Danish cattle. No isolations have been obtained but serological evidence suggests that bovine abortions are caused by leptospires. In 1956, Borg-Petersen and Fennestad[46] reported the isolation of *L. pomona* from a striped field mouse (*Apodemus agrarius*) trapped on a farm where cattle serums reacted to *L. pomona*. One other isolation of *L. pomona* from a mouse (*Mus muscular lusitanicus*) has been reported from Portugal.[47]

Serological studies on domestic animals in Sweden[48] revealed antibodies to either *L. icterohemorrhagiae* or *L. canicola* in 3% of 4,871 dogs, 4.2% of 1,000 pigs, and 12% of 412 horses. Samples from 555 cattle gave inconclusive results according to the author.

Finland is another Scandinavian country that has reported the presence of leptospires. Rislakki and Salminen,[49] found 43.5% of 248 rats (*R. norvegicus, R. rattus*) infected with *L. icterohemorrhagiae*. Leptospires were observed earlier in Finland[50] in the kidneys of silver foxes. This percentage is comparable to the infection rate found in *R. norvegicus* in Norway,[51] Sweden,[52] and most other parts of the world.

Although leptospirosis has been known to occur in the British Isles since 1925 and extensive studies have been undertaken by Broom,[53] Stuart,[54] and Broom and MacIntyre (1948)[55] Field and Sellers[56] and others only two serotypes have been found; namely *L. icterohemorrhagiae* and *L. canicola*. Broom[53] observed a high incidence of Weil's disease among agricultural workers and the number of infections, contracted while swimming in England and Wales but felt that canicola fever was usually found in those persons in a household who have cared for sick dogs rather than as an occupational disease. However, he pointed out that no cases had been observed in other household members indicating close contact with infected dogs as an essential factor in transmission to man. More recently, Coghlan *et al.*[57] in Scotland reported a high incidence of canicola fever in piggery workers and the isolation of *L. canicola* from pigs. Serological surveys revealed canicola antibodies in 40 to 60% of the pig serums examined from several farms. Infected pigs exhibited no symptoms. This high incidence of infection in piggery workers was contrasted with the low infectivity rate observed among dog owners by Broom.[53]

FIGURE 3.



Further, in Austria only two human cases of leptospirosis were diagnosed among the owners of 7,370 infected dogs. There were no cases in the personnel who handled these dogs in the veterinary clinics in Vienna.[55] Recent investigations in the Communicable Disease Center Leptospirosis Research Unit, of leptospirosis in dogs in the Chamblee and Smyrna, Ga. areas provided an opportunity to examine human household contacts of ten cases proved by isolation of *L. canicola*. Examination of serum samples from 50 of these individuals revealed no leptospiral antibodies.

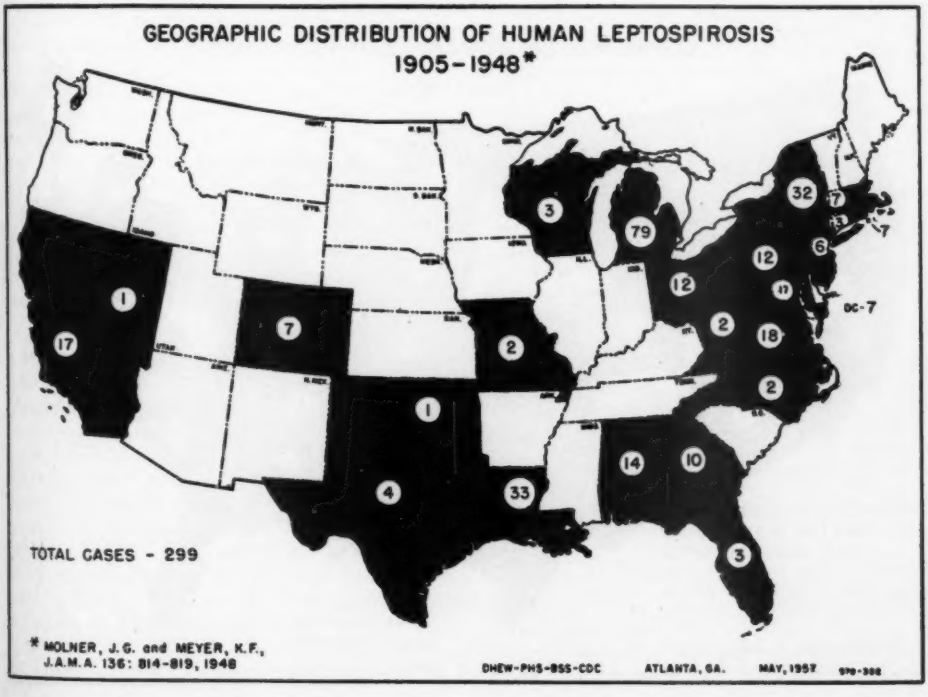
In the Americas, we find only limited reports from South America. Probably the most extensive studies have been undertaken in Argentina where Savino and Renella[59] reported the isolation of *L. hyos* from man and swine and *L. pomona* (described as *L. suis*) from cattle. Similarly in North America reported investigations have been limited except in the United States and Puerto Rico. A recent report from Canada[60] showed that 6% of 1,000 cattle in Ontario and Quebec gave positive complement-fixation tests with *L. pomona* antigen. An occasional human case of leptospirosis has been reported in Canada.[52,54]

Distribution of Leptospires in the United States

Little progress was made in the study of leptospirosis in the United States for some 35 years after Stimson first observed leptospires in kidney sections from a human case in 1905.[3] *L. icterohemorrhagiae* was isolated from rats in New York City by Noguchi in 1917,[5] five years later the first human infection was reported by Wadsworth.[61] A review of the American literature by Larson in 1941[62] revealed 93 reported cases of Weil's disease. Infections with *L. canicola* were first recognized in dogs in 1937 and man in 1938 by Meyer *et al.*[63,64] in California. In recent years many sporadic cases of canicola fever and two rather large water-borne epidemics[25,48] have occurred among human beings. Infections in dogs are widespread. It has been estimated that 25% of dogs in this country have or had leptospirosis and 25 to 50% of these became temporary carriers.[65]

Leptospires were first observed in tissues of cattle by Jungherr[67] in Connecticut. They were first isolated from bovine cases of leptospirosis in New Jersey by Baker and Little[68] and identified as *L. pomona* by Gochenour

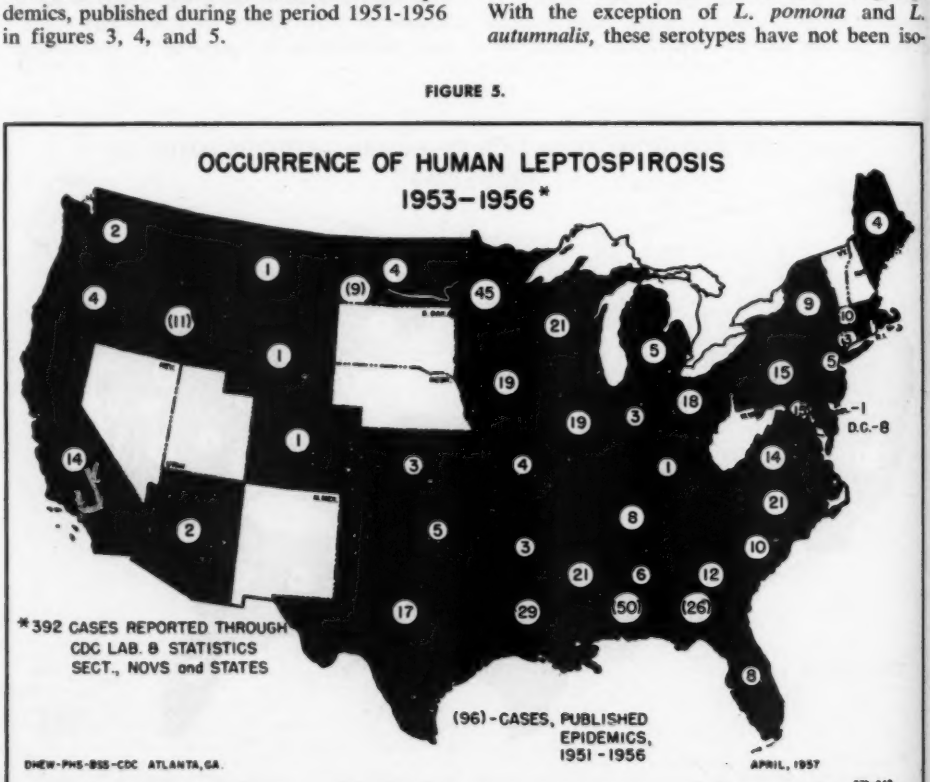
FIGURE 4.


GEOGRAPHIC DISTRIBUTION OF HUMAN LEPTOSPIROSIS
1905-1948*
TOTAL CASES - 299
* MOLNER, J.G. and MEYER, K.F., J.A.M.A. 136: 814-819, 1948
DHEW-PHS-BSS-CDC ATLANTA, GA. MAY, 1957

et al.[69] About this time Beeson[70] reported the first case of "aseptic meningitis" due to *L. pomona* infection. The following year a waterborne outbreak involving about 50 persons due to *L. pomona* was reported by Schaeffer[71] in Alabama. Sporadic cases have been recognized with increasing frequency among abattoir workers and others who have close contact with infected cattle or swine. In 1954, the USDA, A.R.S.[73] estimated that annual losses from bovine leptospirosis are over $112,000,000. or $25,000,000. greater than losses from bovine brucellosis. The rapid spread of bovine leptospirosis in the United States is illustrated in figures 1 and 2 showing the reported occurrence in 1951[72] and the present reported occurrence. The geographic distribution in reported human cases as summarized by Larson[82] in 1941 and by Molner, Meyer and Raskin in 1948[66] is contrasted with those detected during only a four-year period from 1953 through 1956 through serological tests at the Communicable Disease Center laboratory, reported by the C.D.C. Statistics Section of the National Office of Vital Statistics and Epidemics, published during the period 1951-1956 in figures 3, 4, and 5.

While *L. canicola, L. icterohemorrhagiae* and *L. pomona* are the primary infecting serotypes in this country, five other serotypes have been isolated and serological evidence suggests the presence of at least two others. *L. autumnalis* was identified after eight years as the cause of outbreaks in North Carolina during the summers of 1942-43-44 designated as Fort Bragg Fever.[74] *L. ballum* is being isolated frequently from rural house mice and from opossums. Serologic evidence suggests the presence of *L. bataviae* infections in humans,[75] *L. grippotyphosa*[76] in man and cattle and *L. sejoer*[78,81] in cattle. More recently, cultural studies at the C.D.C. Newton, Ga. Field Station[79] on wild mammals trapped in southwest Georgia have yielded a variety of leptospiral serotypes in hitherto unknown hosts including racoons, skunks, and wild cats and also foxes and opossums. The serotypes thus far identified in our laboratory from this source include *L. pomona, L. australis A, L. grippotyphosa, L. autumnalis,* a new serotype belonging to the *mitis-hyos* serogroup tentatively designated *L. bakeri*[80] and a member of the *hebdomadis* serogroup. With the exception of *L. pomona* and *L. autumnalis,* these serotypes have not been iso-

FIGURE 5.


OCCURRENCE OF HUMAN LEPTOSPIROSIS
1953–1956*
*392 CASES REPORTED THROUGH CDC LAB. & STATISTICS SECT., NOVS and STATES
(96) - CASES, PUBLISHED EPIDEMICS, 1951 - 1956
D.C.-8
DHEW-PHS-BSS-CDC ATLANTA, GA.
APRIL, 1957

lated previously in the United States.

All isolates obtained earlier from mice and rats trapped in the same southwest Georgia area proved to be *L. ballum*. Current information regarding occurrence of leptospiral serotypes in the United States is summarized in table 1.

Further studies will be necessary to determine the significance of these findings in regard to the epidemiology of the disease in man and domestic animals. The fact that these types have been identified in the wild animal population of southwest Georgia indicates the need for medical and veterinary laboratories to be prepared to look for them in suspected cases in humans and domestic animals.

Comparison of United States and Foreign Problems in Leptospirosis

In comparing the problems concerning leptospiral infections in man and domestic animals in the United States with those in other countries, the opportunity for exposure must be considered. As has been pointed out, many human infections may be traced to occupational exposure. In Europe, Asia, and Australia, tasks requiring partial immersion in water are usually carried out with no thought to protective clothing. For example in Italy, swineherders clean pens in their bare feet while in the United States farmers usually wear leather shoes or rubber boots for such work. Again abroad, rice-fields are flooded and worked by hand labor, here most of the work is done mechanically. In the United States, it appears that such infections occur only occasionally as sanitation breaks down with certain exceptions. Swimmers in contaminated streams or ponds may become infected in 60-70% of cases. Sporadic cases are seen in livestockmen, abattoir workers, sewer workers, dog owners, or through accidental immersion.

A European physician visiting the Communicable Disease Center recently commented that leptospirosis appears to be primarily a veterinary problem in the United States while in Europe it is a serious human problem. Apparently from our present knowledge of the situation this is true. It would seem that an important influence on this apparent difference may be attributed to more advanced sanitation and mechanization of industrial and agricultural operations. Not to be overlooked, however, is the fact that our knowledge of the true incidence of leptospiral infections in man in the United States is limited. Few medical and public health laboratories provide leptospiral diagnostic services. Diagnosis of the human cases that do come to our attention is based primarily upon serological and clinical evidence. It is estimated that leptospires are isolated from less than 1% of known case in this country. No doubt some mild cases are undetected. Certainly this is a frequent occurrence in dogs and cattle. In view of the success obtained by Australian investigators[81] and Walter Reed Army Institute Research workers[82] with blood cultures on patients with fevers of undetermined origin, every effort should be made to stimulate use of this procedure in our own medical and veterinary hospitals. It is obvious that isolation and identification of leptospires is highly important for further elucidation of the leptospirosis problem in the United States.

REFERENCES

1. Weil, A., Ueber Eine Eigenthumliche, mit Miltztumor, Icterus und Nephritis Einhergenhende, Acute Infectionskrankheit. *Dtsch., Arch. f. klin. Med.*, 30:209, 1886. Cited by Woodward, T., Symposium on the Leptospiroses. Med. Sci. Pub. No. 1, G.P.O., Washington, D. C., 1953, p. 57.

2. Stimson, A. M., A Note on an Organism Found in Yellow Fever Tissue. Pub. Health Rep., 22:541, 1907.

3. Inada, R., Ido, Y., Hoki, R., Kaneko, R., and Ito, H., The Etiology, Mode of Infection, and Specific Therapy of Weil's Disease *(Spirochaetosis Icterohaemorrhagica). Jour. Exp. Med.*, 23:377, 1916.

4. Uhlenhuth, P., and Fromme, W., Weilsche Krankheit. *In. Handb. d. Path. Mikroorg. von Kolle, Kraus and Uhlenhuth.*, 7:487, 1930. Cited by Van Thiel, P. H., The Leptospiroses, Leiden, 1948.

5. Noghuci, H., *Spirochaeta icterhaemorrhagicae* in American Wild Rats and its Relation to the Japanese and European Strains. *Jour. Exp. Med.*, 25:755, 1917.

6. Wolff, J. W., and Broom, J. C., The Genus *Leptospira* Noguchi, 1917. Problems of Classification and a Suggested System Based on Antigenic Analysis. *Documenta de Med. Geog. et Trop.*, 6:78, 1954.

7. Alexander, A. D., Wetmore, P. W., Evans, L. B., Jeffries, H., and Gleiser, C. A., Classification of Leptospiral Isolates from Malaya, Thailand and North Borneo. *Am. Jour. Trop. Med. and Hyg.*, 4:492, 1955.

8. Smith, D. J. W., Brown, H E., Tonge, J. I., Sinnamon, C. N., MacDonald, V. M., Ross, C. J., and Doherty, R. L., The Serological Classification of 89 Strains of *Leptospirae* from North Queensland, Including Five Serotypes new to Australia. *Australasian An. Med.*, 3:98, 1954.

9. Van Riel, P. J., Szpajshendler, L., et Van Riel, M., Etude Clinique, Bacteriologique et Epidemiologique d'un Nouveau Foyer de Leptospirose au Congo Belge. *Bul. Soc. Path. Exotique.*, 49:118, 1956.

10. Broom, J. C., Global Significance of the Leptospiroses. Med. Sci. Pub. No. 1, G.P.O., Washington, D. C., 1953.

11. Kirk, R., Attempts to Demonstrate Leptospirosis in the Northern Sudan. Trans. *Roy. Soc. Trop. Med. Hyg.*, 31:667, 1938. Cited by Van Thiel, P. H., The Leptospiroses, Leiden, 1948.

12. Buchanan, G., Spirochetal Jaundice; Does it Occur in South Africa? *Africa Med. Jour.*, 20:507,

1946. Cited by Austoni, M., Le Leptospirosi, Tipografia del Seminario Di Padova, 1953.

13. Van Riel, J., Recherches sur la Leptospirose du Chein au Congo Belge. *An. Soc. Belge Med. Trop.*, 33:747, 1953.

14. Van Riel, J., Recherches sur la Leptospirose du Porc en Belgique. *Bul. Acad. Roy. Med. Belgique*, 17:368, 1952.

15. Van Riel, J., et M., Recherches sur la Leptospirose Bovine en Aftique Centrale. *An Soc. Belge Med. Trop.*, 35:251, 1955.

16. Bernkopf, H., Olitzki, L., Stuczinski, A., Gotlieb, T., and Halevi, C., Experiments with a Bovine Strain of Leptospira Isolated from a Human Patient. *Jour. Infect. Dis.*, 83:232, 1948.

17. Van der Hoeden, J., The Epidemiology and Epizootiology of Leptospirosis in Israel. *Jour. Trop. Med. Hyg.*, 58:202, 1955.

18. Van der Hoeden, J., Leptospirosis Canicolaris in Pigs and its Probable Transfer to Human Beings. *Jour. Infect. Dis.*, 98:33, 1956.

19. Misao, T., Hiroyoshi, S., Katsuta, K., Nishihara, Y., Kobayashi, Y., Kuwashima, K., and Aso, M., Canicola Fever in Japan. *Am. Jour. Hyg.*, 63:294, 1956.

20. White, E. A., Medical Allied Sciences. Studies of Leptospirosis at the Hygiene Institute in Frankfurt/M. Germany. U. S. Army, 1955.

21. Schlossberger, H., and Brandis, H., Leptospira, *An. Rev. Microbiol.*, 8:133, 1954.

22. Wolff, J. W., and Ruys, A. C., Changes in the Frequency of Weil's Disease in Amsterdam During the Last Eighteen Years. *Documenta de Med. Geog. et Trop.*, 5:247, 1953.

23. Klarenbeek, A., and Schuffner, W. A. P., Appearance in Holland of Leptospira differing from Weil strain. *Nederl. tijdschr. v. geneesk.*, 77:4271, 1933.

24. Collier, W. A., The Verbreitung der Leptospiren in Niede Landische Indien. *Acta. Trop., Basel*, 5:135, 1948.

25. Walch-Sorgdrager, B., Bohlander, H., Schuffner, W., and Wolff, J. W., Serologische Groepeering van Leptospira-stammen, Afkomstig Van Gevallen van Leptospirosis ter Oostkust van Sumatra. *Gen. Tschr. Ned. Ind.*, 80:578, 1940. Cited by Van Thiel, P. H., The Leptospiroses, Leiden, 1948.

26. Esseveld, H., and Collier, W. A., Leptospirosis bij Katten te Batavia. *Med. D. Volksgez. Ned. Ind.*, 27:250, 1938. Cited by Van Thiel, P. H., The Leptospiroses, Leiden, 1948.

27. Fletcher, William, Recent work on Leptospirosis, Tsutsugamushi Disease, and Tropical Typhus in the Federated Malay States. Trans. *Roy. Soc. Trop. Med. Hyg.*, 21:265, 1928.

28. Broom, J. C., Leptospirosis in Tropical Countries. A review, trans. *Roy. Soc. Trop. Med. Hyg.*, 47:273, 1953.

29. Wisseman, C. L., Jr., Traub, R., Gochenour, W. S., Jr., Smadel, J. E., and Lancaster, W. E., Leptospirosis of Man and Animals in Urban, Rural and Jungle Areas of Southeast Asia. *Am. Jour. Trop. Med. Hyg.*, 4:29, 1955.

30. Clayton, G. E. B., Derrick, E. H., and Cilento, R., The Presence of Leptospirosis of a Mild Type (Seven-Day Fever) in Queensland. *Med. Jour. Austral.*, 1:647, 1937.

31. Johnson, D. W., The Australian Leptospiroses. *Med. Jour. Austral.*, Nov. 11, 1950, p. 724.

32. Derrick, E. H., Gordon, D., Ross, C. J., Doherty, R. L., Sinnamon, C. N., MacDonald, V. M., and Kennedy, J. M., Epidemiological Observations on Leptospirosis in North Queensland. *Australasian An. Med.*, 3:85, 1954.

33. Gsell, O., Etiologie der Schweinehuterkrankheit. *Bul. der Schweiz. Aka. Med. Wiss.*, 1:67, 1944.

34. Gsell, O., and Weismann, E., Leptospirosis Typ Mitis. *Schweiz. Med. Wschr.*, 78:503, 1948.

35. Kmety, Emil., Leptospirenforschung in der Slowakei. *Zbl. f. Bakt.*, 161:382, 1954.

36. Kmety, Emil., Leptospirosenherde in der Slowakei. *Zbl. f. Bakt.*, 163:464, 1955.

37. Kmety, Emil, Plesko, Ivan and Chylo, Emanuel., Weitere Ergebnisse der Leptospirosenforschung in der Slowakei. *Zbl. f. Bakt.*, 167:243, 1956.

38. Kemenes, F., Leptospira Infections of Animals in Hungary. *Mag. Allator Lapja*, 11:283, Abs. *Vet. Bul.*, 27:111, 1956.

39. Trbic, B., and Paunovic, S., *Leptospira sejroe* Infection in Dogs. *Acta. Vet.*, Belgrade, 5:79, Abs. *Vet. Bul.*, Dec. 1955.

40. Kirschner, L., Recent Studies on Leptospirosis in New Zealand, Infection With a New Type *(Leptospira mitis)* Johnson (Syn. *Lept. hyos*) in man and Animals. *New Zeal. Med. Jour.*, 53:119, 1954.

41. Babudieri, B., Epidemiology of Leptospirosis in Italian Rice Fields. World Health Organ. Monograph 19. pp. 117. Advance in the control of Zoonoses, Geneva, 1953.

42. Altava, V., Barrera, M., Villalonga, I., Gil, P., Marin, C., Babudieri, B., Vacunacion Como Profilaxis en la Leptospirosis de los Arrozales de Castellon. *Rev. San. Hig. Pub.*, 29: March-April, 1955.

43. Babudieri, B., and Bianchi, L., Untersuchungen uber ein Epidemiches Voskommender Reisfelder Leptospirose in der Provinz Pavia. *Ztschr. f. Imm.*, 98:37, 1940.

44. Borg-Petersen, C., Experience of Leptospirosis in Denmark. *Proc. Roy. Soc. Med.*, 42:714-718, 1949.

45. Fennestad, K. L., Leptospirosis in Domestic Animals. *Nord. Vet. Med.*, 8:325, 1956.

46. Borg-Petersen, C., and Fennestad, K. L., A Field Rodent *(Apodemus agrarius)* as Carrier of *Leptospira pomona* in Denmark. *Jour. Am. Vet. Med. Assn.*, 128:204, 1956.

47. Fraga de Azevodo, J., Valente, J. S., and Quoires, J. J. de S., Novos Dados Sobre as Leptospiras de Portugal. *Anais Inst. Med. Trop.*, 8:621, 1951. Cited by Borg-Petersen in ref. 46.

48. Von Wendt, J., Serological Examinations for Leptospirosis Among Domestic Animals in Sweden. *Nord. Vet. Med.*, 8:711, Abs. *Vet. Bul.*, 27:111, 1957.

49. Rislakki, V., and Salminen, A., Investigations of Leptospirosis in Rats in Finland. *Acta Path. Microbiol. Scand.*, 37:121, 1955.

50. Stenius, P. I., V Nord. Veterinaermode, Sektion 9, Kobenhavn 1939. Cited by Rislakki in ref. 49.

51. Borgen, L. O., Thjotta, Th., Skrift, Norsk. *Videnskapsakad.*, 1:1, 1941. Cited by Rislakki in ref. 49.

52. Malmgren, B., Acta path. Microbiol. Scand., suppl. 43, 1941. Cited by Rislakki in ref. 49.

53. Broom, J. C., Leptospirosis in England and Wales. *Brit. Med. Jour.*, 2:689, 1951.

54. Stuart, R. D., Canine Leptospirosis. *Vet. Rec.*, 58:131, 1946.

55. Broom, J. C., and MacIntyre, A. B., Canine Leptospirosis in England. *Vet. Rec.*, 60:487, 1948.

56. Field, H. J., and Sellers, K. C., Bovine Leptospirosis. *Vet. Rec*, 62:311, 1950.

57. Coghlan, J. D., Norval, J., and Seiler, H. E., Canicola Fever in Man Through Contact with Infected Pigs. *Brit. Med. Jour.*, 1:257, 1957.

58. Advances in the control of Zoonoses. World Health Organization Monograph no. 19, p. 123, 1953.

59. Savino, E., and Renella, E., Leptospiras y Leptospiroses en Argentina. *Dia Med.*, 16:14,43,45, 1944.

60. Moore, T., and Rice, C. E., Serological Investigations of Leptospirosis in Canada. I. Introduction and Preliminary Complement-fixation Studies of Cattle Sera with Commercially-prepared *Leptospira pomona* antigen. *Canad. Jour. Comp. Med.*, 20:362, 1956.

61. Wadsworth, A., Longworthy, H. V., Stewart, F. C., Moore, A. C., and Coleman, M. B., Infectious Jaundice Occurring in New York State. *Jour. Am. Med. Assn.*, 78:1120, 1922.

62. Larson, C. L., Weil's Disease. A Report of 51 Cases Occurring in Puerto Rico and the United States. *Pub. Hlth. Rpts.*, 56:1650, 1941.

63. Meyer, K. F., Eddie, B., and Stewart-Anderson, B., Canine, Murine and Human Leptospirosis in California. *Proc. Soc. Exper. Biol. Med.*, 38:17, 1938.

64. Meyer, K. F., Stewart-Anderson, B., and Eddie, B., Canicola Fever—A professional Hazard. *Jour. Am. Vet. Med. Assn.*, 46:332, 1938.

65. Williams, H. R., Murphy, W. J., McCroan, J. E., Starr, L. E., and Ward, M. K., An Epidemic of Canicola Fever in Man with the Demonstration of *Leptospira canicola* Infection in Dogs, Swine and Cattle. *Am. Jour. Hyg.*, 64:46, 1956.

66. Cockburn, T. A., Vavra, J. D., Spencer, S. S., Dann, J. R., Peterson, L. J., and Reinhard, K. R., Human Leptospirosis Associated with a Swimming Pool, Diagnosed After Eleven Years. *Am. Jour. Hyg.*, 60:1, 1954.

67. Jungherr, E., Bovine Leptospirosis. *Jour. Am. Vet. Med. Assn.*, 105:276, 1944.

68. Baker, J. A., and Little, R. B., Leptospirosis in Cattle. *Jour. Exper. Med.*, 88:295, 1948.

69. Gochenour, W. S., Jr., Yager, R. H., and Wetmore, P. W., Antigenic Similarity of Bovine Strains of Leptospirae (United States) and *Leptospira pomona*. *Proc. Soc. Exper. Biol. Med.*, 74:199, 1950.

70. Beeson, P. B., Hankey, D. D., and Cooper, C. F., Leptospiral Iridocyclitis. Evidence of Human Infection with *Leptospira pomona* in the United States. *Jour. Am. Med. Assn.*, 145:229, 1951.

71. Schaeffer, M., Leptospiral Meningitis. Investigation of a Waterborne Epidemic due to *L. pomona*. *Jour. Clin. Investigation*, 30:670, 1951.

72. York, C. J., Aspects of Control in Bovine Leptospirosis. Proc. 55th An. Meeting, U. S. Livestock San. Assn., Kansas City, 1951.

73. U. S. Department of Agriculture, Agri. Res. Ser. Losses in Agriculture, A Preliminary Appraisal for Review, 1954, p. 129.

74. Gochenour, W. S., Jr., Smadel, J. E., Jackson, E. B., Evans, L. B., and Yager, R. H., Leptospiral Etiology of Fort Bragg Fever. *Pub. Hlth. Rpts.* 67:811, 1952.

75. Gochenour, W. S., Jr., Yager, R. H., Wetmore, P. W., Evans, L. B., Byrne, R. J., Alexander, A., and Hightower, J. A., Indonesian Weil's Disease in Puerto Rico and the United States. *Federation Proc.*, 10:408, 1951.

76. Spain, R. S., and Howard, G. T., Leptospirosis due to *Leptospira grippotyphosa*. *Jour. Am. Med. Assn.*, 150:1010, 1952.

77. Galton, M. M., Acree, J. A., Lewis, A., and Prather, E. C., Leptospirosis in Domestic Animals in Florida with Reference to Cattle. *Jour. Am. Vet. Med. Assn.*, 128:87, 1956.

78. Yager, R. H., Leptospirosis in the United States Today. Med. Sci. Pub. No. 1, 1952, p. 221.

79. McKeever, S., Gorman, G. W., Chapman, J. F., Galton, M. M., and Powers, D. K., New Records of Leptospiral Infections in Feral Mammals from Southwestern Georgia. To be published.

80. Galton, M. M., Powers, D. K., McKeever, S., and Gorman, G. W., The Identification of Two Leptospiral Serotypes New to the United States. Pub. Hlth. Rpts., 72:431, 1957.

81. Ross, Cynthia J., Blood Culture in the Diagnosis of Leptospirosis in North Queensland. *Med. Jour. Austral.*, August, 1955, p. 319.

82. Alexander, A. D., Walter Reed Army Inst. of Research, Washington, D. C., personal communication, 1956.

83. Saint-Martin, M., and Carbbonneau, J. H. Meningitis due to *Leptospira canicola:* First Report of Occurrence in Canada. *Canad. Med. Assn. Jour.*, 73:454, 1955.

84. Bourne, F. Munroe., Leptospirosis sejore with a case report. *Canad. Med. Assn. Jour.*, 73:886, 1955.

85. Rosenburg, B. L., Canicola Fever, Review with report of two new cases. *Am. Jour. Med.*, 11:75, 1951.

86. Molner, J. G., Meyer, K. F. and Raskin, H. A., Leptospiral infections, a survey *Jour. Am. Med. Assn.*, 136:814, 1948.

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Anthelmintic Properties of Papain

Papain, a proteolytic enzyme, is the dried and purified latex from a papaya much used in the United States as a meat tenderizer. It is recommended by Drezancic of Yugoslavia, in an article published in the *Australian Veterinary Journal* for July 1957, as an anthelmintic for stomach worms in sheep. Papain is a protein digestant; its action is said to be due to the liberation of histamine so as to embarrass vitality of tissues depending upon a vascular supply. Drezancic administered from 5 to 10 gm. in 60 ml. of water directly into the abomasum with the result that in some of the experimental animals no worms were found on a postmortem examination. More important, 90% or more of the eggs were digested in a short time.

In the summary the author states, "It has some advantages over other anthelmintics as it is not toxic to the host and can be administered safely to young, sick, or weak animals, and to those in advanced pregnancy. Its ability to destroy the ova of *H. contortus* as well as the worms is of importance in the reduction of contamination of the pastures." — *R. R. Dykstra, D.V.M.*

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Diagnosis of metabolic diseases that may arise from improper, inadequate, or unbalanced feeding requires that the attending veterinarian be appraised of all recent nutrition changes advanced and recommended.

Epidemiologic And Public Health Aspects Of Leptospirosis†

FRED R. McCRUMB, JR.,* M.D., Baltimore, Maryland

SINCE the discovery of Miyajima in 1915,[1] that field mice may harbor the spirochetes of nanukayami or leptospirosis hebdomadis, numerous workers have established the relationship between rodent reservoirs and human leptospirosis. In the light of epidemiologic studies conducted during the past 35 years, it seems reasonable to assume that the leptospiroses originated in long-standing endemic foci of the tropics, as for example, southeast Asia where, even today, the richest leptospiral flora is to be found. When migration to Europe, Australia, and North America occurred, the spread of certain serotypes was limited by unsuitable rodent hosts or an unfavorable external environment and as the cultivation of land by man led to further selection of rodent hosts, fewer leptospiral types became established. As the interrelationships among rodents, external environment and man varied from region to region, so did the numbers and types of leptospires.

The formation of endemic foci is affected by many factors only some of which are known. First, there must be suitable non-immune rodent populations to maintain the life cycle of leptospires; the richer the rodent fauna the more diversified the leptospiral flora. Second, conditions must be conducive to the survival of leptospires outside of the rodent body. Finally, there must be habitual contact between man and rodent reservoirs through the medium of naturally occurring water. The first two of these factors are virtually unexplored problems and, in spite of much conjecture based on incomplete experiments and chance observations, those attributes which make one rodent a good host and another a bad one, as well as those requirements demanded of the external environment by the leptospire, are for the most part undefined.

TABLE 1. Rodent Reservoirs of Leptospires

Endemic region	Rodent hosts	Leptospiral serotypes
Italy	*Micromys min. sorcinus*	*L. bataviae*
	Apodemus spp.	*L. icterohemorrhagiae*
	Rattus norvegicus	
United Kingdom	*Rattus norvegicus*	*L. icterohemorrhagiae*
Japan	*Microtus montebelli*	*L. canicola*
		L. hebdomadis
	Apodemus s. speciosus	*L. autumnalis*
Malaya	*Rattus norvegicus*	*L. pyrogenes*
	Rattus diardii	*L. hebdomadis*
	Rattus jalorensis	*L. bataviae*
	Rattus argentiventer	*L. grippotyphosa*
	Rattus exulans	*L. schuffneri*
	Rattus mulleri	*L. javanica*
	Rattus bowersi	*L. icterohemorrhagiae*

Each endemic area has its special features, and factors which apply to one area may not be operative in another. For this reason, epidemiology of leptospirosis must be defined in terms of local conditions and not by a set of general rules to be applied on a world-wide basis. The complexity of this problem is illustrated in table 1 where reservoirs and leptospiral types encountered in several endemic areas are listed. The contrast between fairly simple, specialized situations, as in Italy and the United Kingdom, and multiple-serotypic foci as in Malaya is conspicuous. Furthermore, the relationship which exists between a varied rodent fauna and the occurrence of numerous serologically distinct leptospires is quite clear.

As time does not permit consideration of the epidemiologic aspects of leptospirosis in more than a few regions, two examples (Italy and Malaya) have been chosen for detailed comments. At the end of the discussion an attempt will be made to compare these observations with the current status of our knowledge regarding leptospirosis in the United States.

†Presented at the Interprofessional Symposium on Leptospirosis. Postgraduate Medical Study, University of Kansas Medical Center, Kansas City, Kansas, April 25, 1957.

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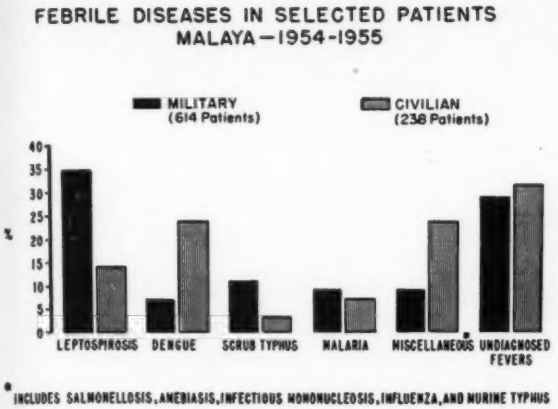

Figure 1.

Leptospirosis in Italy

Leptospirosis occurs with great regularity among rice-field workers in Italy. This problem has been studied by several investigators, among them Mino and Babudieri, and the data to be presented in this regard have been taken from work done by Prof. Babudieri and his coworkers.[8] Rice cultivation in Italy is restricted almost exclusively to the Po Valley where it is estimated that 600,000 persons are engaged in this work each year. Sowing of rice takes place in April after which the ground is irrigated by a system of canals. In June, the *monda* or cleaning takes place at which time workers may spend an entire day with bared feet and legs submerged in water. Cases of leptospirosis occur at this time and again in September and October when the crop is harvested. During the harvest, the ground is covered with pools of water and ripe grain attracts large numbers of field rodents. Although the commonest rodent encountered is *Micromys minutus sorcinus* (dwarf mouse), Apodemus spp. may also be present. While several leptospiral serotypes have been encountered in human infection, 80 to 90% are caused by *Leptospira bataviae* and *L. icterohemorrhagiae*. Selective survival of these serotypes seems to have been a function of the restricted rodent fauna since only these serotypes can be isolated with great regularity from the field mice. *L. grippotyphosa*, common elsewhere in Europe, is rare in Italy where its established reservoir *Microtus arvalis* does not occur. The relationship of rice-field work and leptospirosis has been established in this region where leptospiral antibody rates have been shown to increase with length of service in this occupation.

I would like to emphasize at this point that the age, sex, and seasonal distribution of this disease in Italy is strictly a function of man's habits and has nothing to do with curious predilections of the leptospires. Thus, a disease frequently associated with males in other areas is seen in females in Italy simply because many of the *mondine* workers and harvesters are women. Similarly, the peaks of this infection are noted in June and September because it is at this time that workers are in contact with contaminated water. It is obvious therefore that age, sex, and seasonal factors noted in Italy may not apply in other regions where the epidemiology of leptospiral infection is not associated with rice growing or where rice growing is carried out in a different fashion.

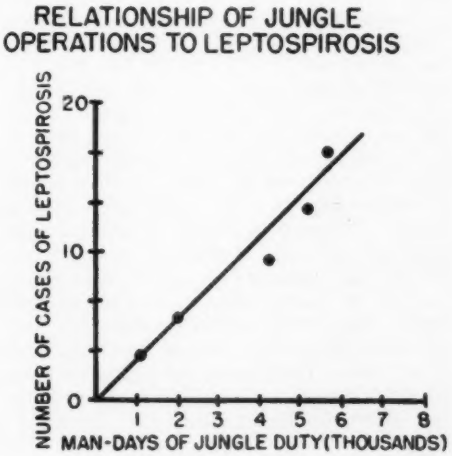

Fig. 2. Jungle leptospirosis.

In Malaya, the situation is much more complex. Leptospirosis has been recognized in that country since 1928 when William Fletcher [3] isolated the causative organism from the blood of a rubber tapper ill with an unexplained fever. He showed further that several species of rats were naturally infected and that dogs could shed leptospires in their urine. Studies on leptospirosis in Malaya ceased with the retirement of Fletcher and it was not until several years ago when anticommunist operations exposed many European soldiers to these long-established endemic foci of leptospiral infection that interest in this disease was revived. During 1954-55 it was our privilege to investigate the causes of various fevers among foreign military personnel and indigenous civilians in Malaya.[4] The results of this study of over 800 patients reveal that leptospirosis was a particularly serious problem among troops (fig. 1). Observations of the habits of these patients provided additional support for the concept earlier expressed by Fletcher that exposure to leptospires could occur in urban and cultivated rural areas as well as scrub and primary forest in Malaya. In the present investigation the frequent appearance of this disease among men whose occupation took them into jungle (that is, anticommunist military personnel) suggests that this particular environment represents one of the important permanent foci of leptospiral infection in Malaya. This is by no means the only source of leptospiral infection, however, since most of the indigenous patients were employed in agricultural or mining pursuits in cultivated areas. Because leptospirosis did present a serious problem to the military, and because the concept of a permanent jungle leptospiral reservoir had received little attention in previous studies, it was deemed worthwhile to emphasize this aspect of leptospirosis in Malaya. A brief description of the topography of Malaya and the nature of jungle operations may be in order at this time. Malaya is part of a peninsula and is itself about 500 miles in length. There is a central mountain range running from north to south which effectively divides the east and west coasts. Three-quarters of this country is clad with virgin tropical rain forest which contains innumerable streams, marshy lowlands and a rich rodent fauna. The annual rainfall varies from 80 to 100 inches and is fairly evenly distributed throughout the 12 months.

Jungle operations were usually carried out with units of platoon strength. Men assembled

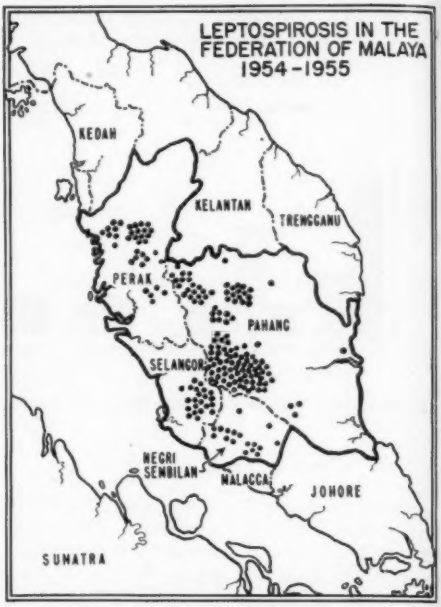

Fig. 3. Geographic distribution of leptospirosis in Malaya, 1954-1955.

on the first day of a jungle operation were frequently helicoptered into deep forest. Depending on the mission, they were expected to stay in the jungle for one to 30 days where they operated from base camps usually occupied only once. During this time there was repeated exposure to streams, stagnant pools and pig wallows. The occurrence of skin abrasions from underbrush as well as leech bites probably made exposure to leptospires even more hazardous although the consumption of contaminated drinking water could not be overlooked as a means of infection.

Detailed study of the habits of these men left little doubt that most of the leptospiral infections were contracted in the jungle. Not only was leptospirosis confined to operational troops as opposed to support units, but there was a clear-cut relationship between time spent in jungle and the incidence of infection (fig. 2). In addition however, it soon became apparent that all jungle areas did not present the same risk of infection. Thus well-known hyperendemic foci became common topics of conversation among the troops and indeed the concentration of cases in certain endemic regions in western and northwestern Pahang was obvious (fig. 3).

While the circumstances which lead to the establishment of rodent reservoirs in jungle,

rural and urban areas of Malaya are not known, it is well established that rodents from all three environments can be infected with leptospires and that several different leptospiral serotypes may co-exist within a radius of a few thousand yards. Here again the entrance of man into the cycle is accidental and the epidemiology of this disease is defined in terms of man's activities, be he rubber tapper, tin miner, or jungle fighter.

Leptospirosis in the United States

Of more practical value, what do we know about leptospirosis in the United States? For a variety of reasons, leptospirosis has been regarded by most American physicians as a tropical disease and, until recently, consideration of rodent reservoirs has not advanced beyond the survey of *Rattus norvegicus* in most regions of this country. Since 1922, less than 500 cases of leptospirosis of the *L. icterohemorrhagiae* variety have been recorded. In 1938 Meyer[5] described human infection with *L. canicola* but by 1951 only 13 cases of this variety had been reported in this country. In 1948, it was established that bovine leptospirosis could be caused by *L. pomona*[6] and, since that time, human infection caused by this serotype has been recognized. It was further demonstrated that horses and swine could also become naturally infected with this serotype. Subsequently, it was shown that *L. autumnalis, L. bataviae* and *L. grippotyphosa* may produce disease in this country. At the present time there is little doubt that at least *L. pomona* infections in cattle and swine and *L. canicola* infection in dogs represent serious problems. It is not as clearly established however, that the low reported incidence of human leptospirosis is solely a function of misdiagnosis. For example, numerous surveys of *Rattus norvegicus* have shown the carrier rate of *L. icterohemorrhagiae* to be as high as 50% in adult rats. In a city such as Baltimore where this situation exists, it is much more likely that city dwellers are not exposed to excreted leptospires under conditions which would favor infections. This concept is further supported by a low incidence of leptospiral antibody among adult urban dwellers. Outside of heavily populated areas however, mild forms of leptospirosis could readily escape detection and it is in the rural areas that a diversified rodent fauna would be more conducive to the establishment of serotypes other than *L. icterohemorrhagiae*. Whatever the explanation, these questions can only be solved by careful investigation of human and domestic animal illnesses as well as rodent reservoirs of all types. Diagnostic methods are within the scope of many laboratories where they are not currently employed and the insistence of physicians, veterinarians and public health workers that they be made available will hasten their acceptance.

Summary

In summary, we must be cognizant of certain established facts in order to understand the epidemiologic aspects of the leptospiroses wherever they occur. (1) Leptospirosis is primarily a disease of rodents and it is upon these hosts that the leptospires depend for their survival. (2) Man and his domestic animals become infected quite by accident and although certain leptospiral serotypes have become more or less well adapted to domestic animals, with few exceptions, such as in the case of *L. pomona* and *L. canicola*, this secondary cycle is still probably a minor one in terms of permanent natural reservoirs. (3) Leptospiral infection in man is dependant upon his coming in contact with excreted leptospires in the course of his daily life. (4) Finally, the epidemiology of leptospiral infection which varies from one endemic area to another seems to be governed to a great extent by the availability of suitable rodent hosts and an external environment favorable to the survival of leptospires.

REFERENCES

1. Van Thiel, P. H., The Leptospiroses. Univ. Pers. Leiden, 1948.

2. Babudieri, B., Epidemiology of Leptospirosis in Italian Rice Fields. WHO Monograph Series No. 19. Advances in the Control of Zoonoses, 117, 1953.

3. Fletcher, William, Recent Work on Leptospirosis, Tsutsugamushi Diseases and Tropical Typhus in the Federated Malay States. (Trans.) *Royal Soc. Trop. Med. and Hyg.*, 21:265, 1928.

4. McCrumb, F. R., Stockard, J. L., Robinson, C. R., Turner, L. H., Levis, D. G., Kelleher, M. F., Gleiser, C. A., and Smadel, J. E., Leptospirosis in Malaya. I. Sporadic Cases among Military and Civilian Personnel. *Am. Jour. Trop. Med. Hyg.*, In press.

5. Meyer, K. F., Stewart-Anderson, B., and Eddie, B., "Canicola fever," A Professional Hazard. *Jour. Am. Vet. Med. Assn.*, 46:332, 1938.

6. Baker, J. A., and Little, R. B., Leptospirosis in Cattle. *Jour. Exper. Med.*, 88:295, 1948.

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"Orphan" viruses are so designated because no illness is produced when injected into laboratory animals, or the diseases to which they belong are unknown.

Some Tissue Alterations In Man Caused By Leptospira†

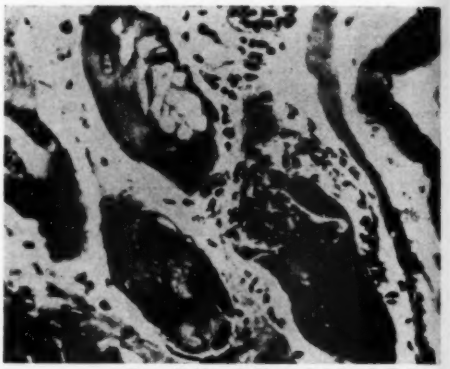
JOHN T. LOGUE,* M.D., Columbia, Missouri

IN man, the clinical syndromes caused by leptospiral organisms vary from isolated iridocyclitis, benign febrile episodes that most often pass undiagnosed, to a more severe febrile meningitis and then to classical Weil's disease which is manifested by signs of increasingly severe hepatic and renal failure.

Before viewing some of the tissue alterations caused by invasion of the human body by the leptospiral organism, I would like to direct your attention to table 1, which compares the reported instances of selected infectious diseases and their mortality rates from 1947 through 1954. From these figures, it is apparent that only the severe forms of leptospirosis are being reported. It is equally apparent that our therapeutic efforts are not yet as successful as they are in other infectious diseases. Specific therapy with antisera, antibiotics, and good supportive care have yet to reduce the mortality rate to an acceptable level. Perhaps the judicious use of the artificial kidney in the anuric stage of the fatal form of this disease will increase the salvage rate as it has done in other forms of so-called lower nephron nephrosis.

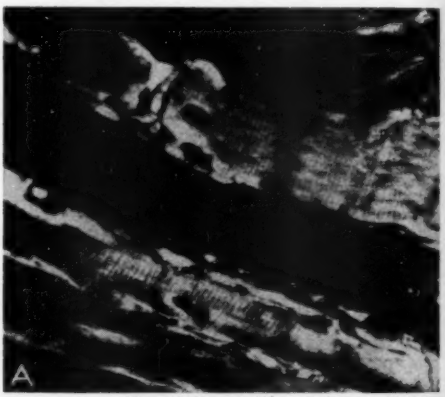
Pathological studies are incomplete in cases of non-fatal leptospirosis, with the exception of serial studies of acute and convalescent gastrocnemius muscle from cases of *spirochetosis icterohemorrhagica.* This interesting study was carried out by Dr. W. H. Sheldon[1] of Emory University.

The earliest discernible change is the formation of vacuoles within the cytoplasm of the striated muscle fiber with the loss of cross striations, followed by the appearance of multiple nuclei in the uninvolved portions of and localized hemorrhage into the muscle fibers. This is followed by the appearance of cells displaying characteristics of sarcoblasts. Small numbers of polymorphonuclear leukocytes are



From Sheldon—Archives of Internal Medicine.

Fig. 1. Acute alterations in the human gastrocnemius muscle due to spirochetal jaundice.



From Sheldon—Archives of Internal Medicine.

Fig. 2. Muscle regeneration in convalescent human gastrocnemius muscle from case of spirochetal jaundice (Weil's disease).

TABLE 1. Reported Cases and Deaths in Selected Infectious Diseases 1947-1954*

	Brucellosis	Tularemia	Psittacosis	Q Fever	Leptospirosis
Cases	28,588	7165	1012	30	249
Deaths	307	165	14	0	134
% Fatalities	1.1	2.3	1.4	0	53.8

*Date from Biological Handbook, Saunders, 1957.

†Presented at the Interprofessional symposium on Leptospirosis. Postgraduate Medical Study, Kansas University School of Medicine, Kansas City, Kansas, Apr. 25, 1957.

*Clinical Associate in Medicine, University of Missouri School of Medicine.

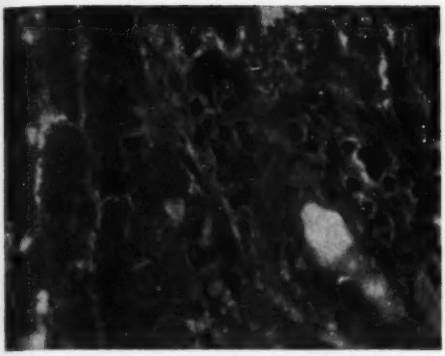


Fig. 3. Human canicola fever. Liver: Note cloudy swelling of liver cells, nuclear variation, and periportal inflammatory reaction.

observed. (Fig. 1.) This stage is followed by signs of muscle regeneration. (Fig. 2.)

Pathologic studies from fatal cases of leptospirosis reveal rather uniform, though nonspecific tissue reactions regardless of the type of leptospiral organism involved.

Grossly, jaundice is usually apparent. It may be mild, limited to the sclera, or may be deep in intensity, staining the skin and the organs of the body. Hemorrhages in the serous membranes, usually in the form of petechiae, and ecchymoses, are quite common. Hemorrhage has been described in the epicardium, pleura, skeletal muscle, gums, conjunctiva, skin, liver, kidneys, heart, stomach, and small intestine.

The kidneys are usually enlarged and capsules strip with ease revealing petechial hemorrhage over the cortex. The liver is usually enlarged and bile stained. The extra-hepatic bile passages and gallbladder are normal. The spleen may be normal in size, but sometimes enlarged in autopsied cases.

Figures 3 and 4 of liver, and kidney respectively are from a case of canicola fever in a 26-year-old male who died on the tenth day of his illness after a typical clinical course. On the day before death, agglutinations were:

Positive for *L. icterohemorrhagiae*	1:512
Positive for *L. canicola*	1:2048
Positive for *L. pomona*	1:512

Serum bilirubin and blood NPN were elevated.

Microscopically, the predominant lesions seem to be focal interstitial infiltrations of lymphocytes and plasma cells, presumably at the site of invasion of the organ cells by the Leptospira. Depending on the age of the insult, one may also see signs of cellular necrosis and regeneration associated with the interstitial infiltrations. These changes are most prominent in the skeletal muscle, the liver and the kidneys, but may be found in any of the body organs.

On microscopic sections of the liver, one sees cloudy swelling of the liver cells with dissociation of the liver cords, double nuclei with variation in nuclear size, including the characteristic giant nuclei in the polyagonal cells, enlargement of Kupffer cells, inspissated bile in the biliary canaliculi, (fig. 3), and diffuse hemorrhage. With special staining technics one may demonstrate leptospiral organisms in the tissue, (fig. 5).

The spleen shows reticuloendothelial hyperplasia with increase in the number of neutrophiles.

The most characteristic microscopic changes in leptospirosis are found in the kidneys and consist of:

1. An interstitial non-suppurative inflammatory infiltration of the cortex and medulla consisting mostly of lymphocytes and plasma cells. (Fig. 4.)

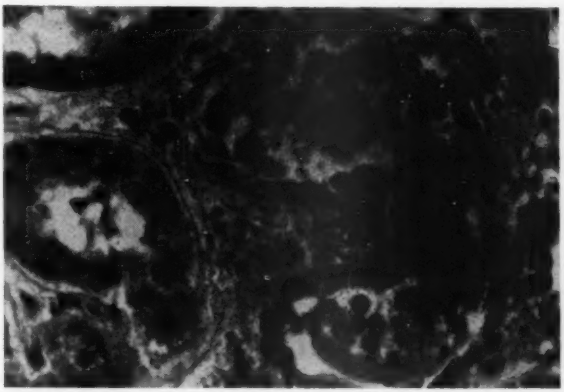
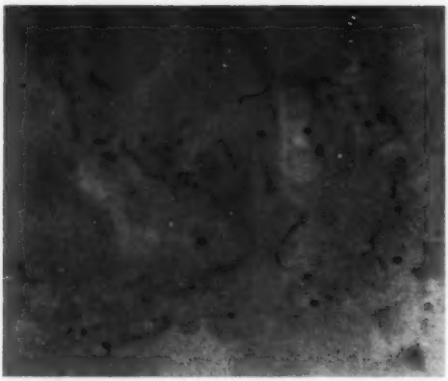
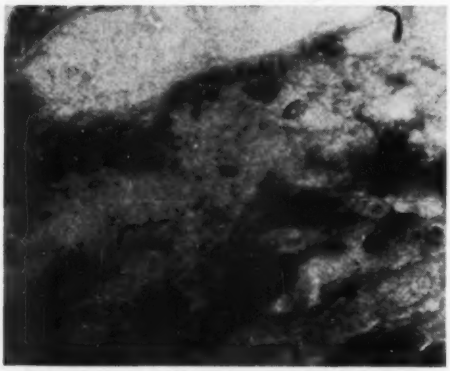


Fig. 4. Human canicola fever. Kidney: Note tubular changes.



Adapted from **Color Atlas of Pathology**, J. B. Lippincott Company.

Fig. 5. Human liver showing Leptospira, (Levaditi stain).



From Koppisch, et. al., **The Morbid Anatomy of Human Leptospirosis**. Medical Science Publication no. 1: 83-104, 1952.

Fig. 6. Leptospira in renal tubule.

2. Focal or generalized edema of the cortex.
3. Cloudy swelling of the tubules.
4. Hyaline and desquamated cellular casts.
5. Protein in the tubular lumen.
6. Dilatation of the distal and collecting tubules.

Glomerular alterations are usually mild, consisting of thickening of the basement membranes and cloudy swelling of the capsular epithelium. Leptospira, when they can be demonstrated, are usually found in all levels of the kidney tubules. The organisms can rarely be demonstrated in the kidney parenchyma by the usual staining technics. (Fig. 6.)

The tissue alterations in the human body caused by the various types of Leptospira are non-specific, and unless the organisms are either positively identified in the tissues, by using special staining technics or are recovered from the body and identified bacteriologically, the pathological diagnosis can not be made with certainty. The close resemblance of the kidney lesions produced by Leptospira to the so-called lower nephron nephrosis which follows extensive trauma leads one to wonder about the possibility of using the artificial kidney in treating anuric patients with Weil's disease.

REFERENCE

1. Sheldon, W. H., Lesions of Muscle in Spirochetal Jaundice (Weils Disease: Spirochetosis icterohemorrhagica). *Arch. Int. Med.*, 75:119, 1945.

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Porcine Semen Life

Unlike semen from bulls, sperm from boars is destroyed by freezing under any method currently known.

Scientists at the USDA Beltsville station have succeeded in extending boar semen life to about 50 hours, according to recent announcement. Among others finding it was determined that best results were obtained when the selected portion was treated and a diluent added and then stored at temperatures within the range of 59 and 68 F.

The matter of swine semen storage is of particular significance at present because of pressures exerted for production of market swine having desirable characteristics of rapid and economical growth and finish without excessive fat or proportion of fat to lean.

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Proper Milking for Mastitis Prevention

Insufficient attention is given at least two important factors in the etiology of bovine mastitis; both concern milking management. (1) Forcible removal of the teat cups when suction is still active, or at least not entirely suppressed, causes eversion of the lining of the teat, and if repeated often enough, invites infection. (2) Also, it has been demonstrated at the University of Connecticut that leaving the milking machine active for excessive duration — the average time as determined by the Animal Husbandry Dept., New York State College of Agriculture should be slightly over three and one-half minutes — resulted in a leukocyte change and chloride content, both signs of mastitis.—*R. R. Dykstra, D.V.M.*

Leptospirosis Of Domestic Livestock†

HAROLD S. BRYAN,* D.V.M., Ph.D., Kalamazoo, Michigan

PERSONAL experience with leptospirosis was acquired at the College of Veterinary Medicine, University of Illinois, Urbana, where the writer was associated until last year.

Leptospirosis is not a new disease in the United States, but apparently can be referred to as a newly recognized disease. It has only been during the past five years that research workers and veterinarians have been making diagnoses of this condition in livestock with regularity. Yet, today we recognize leptospirosis as causing, as you have heard, a $100,000,000. loss among livestock annually in the United States. Thousands of cattle and hogs are involved each year. Economic and veterinary importance of this disease has been grossly underestimated, at least in this country. Perhaps this is also true currently in human medicine. We have heard that there are approximately eight or nine serotypes or species of leptospires which occur in this country. Nearly all of these have been found in animals. For the sake of brevity, I would like to limit my discussion to *Leptospira pomona* infection as it occurs in domestic livestock. This organism causes disease difficulty in cattle, hogs, sheep, and horses and perhaps other animals.

The discussion centers about the disease as it occurs in cattle and hogs primarily and as the condition has been observed in Illinois. Serologically speaking, using the agglutination-lysis test, the disease involves about 30% of the cattle and swine herds and nearly 20% of the cattle and swine. This is stated merely to emphasize that there is a rather high incidence of *L. pomona* infection in Illinois.

From the historical viewpoint, it was 1944 when Jungherr first described the disease in cattle in the United States. In Illinois, it was 1948 when Doctors Sutherland and Morrill first described the condition; the outbreak occurred in a herd of beef cattle. In this particular herd several adult cows died and some pregnant cows aborted. In 1955, *L. pomona* was isolated from aborted bovine fetuses by workers at the Storrs Agricultural Experiment Station. In 1950, Bohl and Ferguson reported serological evidence of *L. pomona* infection in swine. *L. pomona* was isolated from aborted swine fetuses for the first time in the United States at the University of Illinois in 1953. Reports of leptospirosis in sheep are sparse, but serological evidence of the disease in this animal species has been reported. U. S. Army workers in 1950 reported serological evidence of *L. pomona* infection in horses and also intimated that this organism was the cause of periodic ophthalmia or moon blindness.

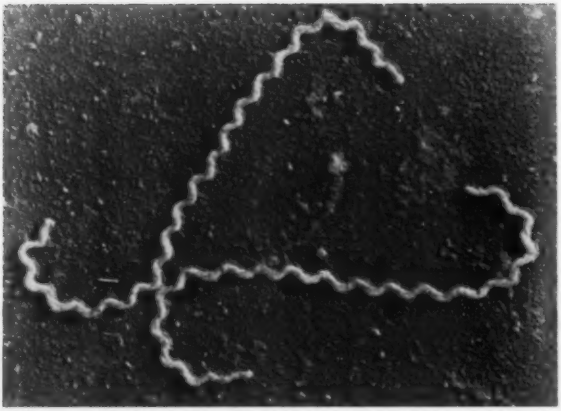
Signs of Illness Due to Leptospira

What are the signs or symptoms of the illness in cattle or swine? We recognize that leptospirosis is primarily a herd problem, and that when the disease first enters a herd it is almost impossible to predict the exact course which it will take. The signs of the disease are quite variable and may be of an acute or chronic nature. Within a single herd, symptoms can be light or not apparent at all or they can be quite severe. Inapparent cases

†Presented at the Interprofessional Symposium on Leptospirosis, Postgraduate Medical Study, University of Kansas Medical Center, Kansas City, Kansas, April 25, 1957.

*Veterinary Research and Development Section, The Upjohn Company.

Kidney lesions of bovine leptospirosis. Note areas of necrosis (white spots) which are chpracteristic autopsy findings in advanced cases.



Two *Leptospira pomona* organisms as seen with the electron microscope, magnified approximately 9,000 times. Note the closely-spiralled, cylindrical organisms with hooked ends.

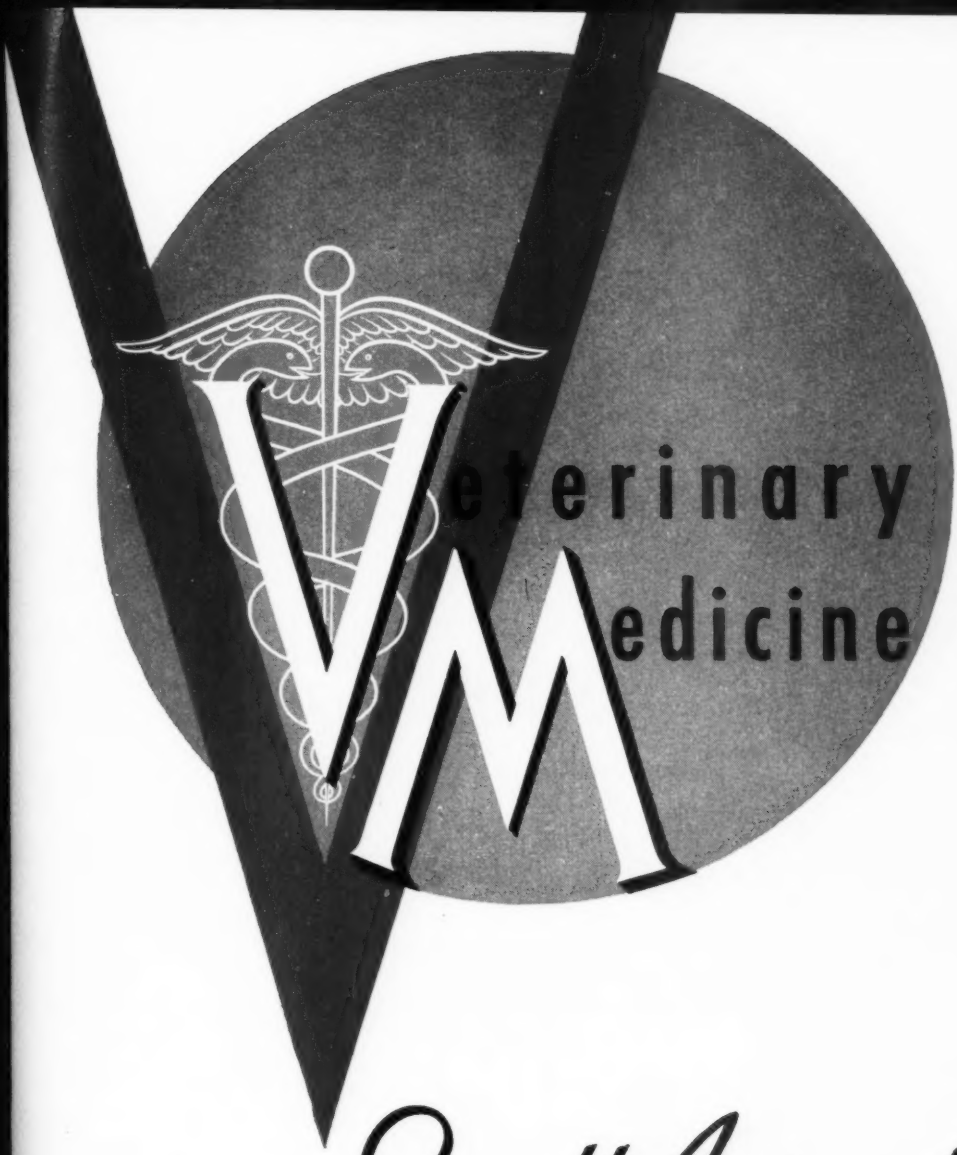
Photo courtesy H. E. Rhoades and A. E. Vatter.

can be detected only by serological tests. Of the symptoms then, the outstanding one is premature birth of the young, both in cattle and in swine. A sudden reduction in milk flow in dairy cows may occur. The secretion that one can obtain from the mammary gland is frequently of a thick, yellowish nature and may be blood tinged. Veterinarians speak of these cases as they occur in dairy herds as cases of "soft" mastitis. Other symptoms include fever, anorexia, hemoglobinuria, anemia, and icterus. Morbidity approaches 100% in a typical herd outbreak. Mortality is usually low, 5% or less, losses occur mainly in young stock. Abortion may occur in 15 to 20% of the pregnant cows when the disease first strikes a herd but in swine up to 100% of the pregnant sows may abort. Sows usually abort two to four weeks before term; cows, at any stage of pregnancy. When symptoms are of an acute nature, leptospirosis may be confused with diseases or conditions such as anaplasmosis and plant and chemical poisoning. Occasionally, hemolytic infections such as pyelonephritis and bacillary hemoglobinuria caused by *Clostridium hemolyticum* must be ruled out. In cases of abortion, brucellosis, vibriosis, trichomoniasis are infections that may confuse. In chronic cases, one may have to rule out parasitism and malnutrition in that there may be general unthriftiness and poor weight gain. The practitioner must have and certainly wants laboratory confirmation of his diagnosis. More and better diagnostic facilities are required to meet the need for confirming clinically diagnosed cases.

Introduction of Infection

Leptospirosis is frequently introduced into a herd through the addition of an apparently healthy carrier animal. Urine from chronic carriers serves as the chief source of infection for susceptible animals. Infection usually occurs through the mucous membranes of the eyes, nose, throat, and vagina but the organism can also enter through cuts and abrasions of the skin. Infection may also spread through contact with urine contaminated bedding or organisms present in poorly drained pastures, ponds, or streams. What role does semen play in the dissemination or transmission of the disease? Realizing that leptospirosis in its chronic form involves the kidney, organisms may be eliminated from the body in the urine, and since semen uses the same channel, it is not difficult to see how semen could become contaminated. Thus an infected herd sire could aid materially in the dissemination of the disease, and in fact many herd outbreaks can be traced to new additions of sires, especially boars. Concerning the role which milk plays in the transmission, one should recall the work of Baker and Little when they isolated Leptospira from milk. This emphasizes the fact that organisms might appear in milk. However, there is also another report in the literature indicating that leptospires do not survive well in fresh raw milk. Pasteurized milk is safe as leptospires are extremely sensitive to heat. Rodents have been mentioned as infective carriers, but it appears that they do not play an important role in the transmission of *L. pomona* to cattle and swine. Much more important is the reservoir of infection in swine.

Successful prevention of leptospirosis depends upon avoiding the introduction of the disease into a healthy herd. A leptospirosis blood test of newly purchased animals is an important factor in good herd management. Vaccination of susceptible cattle and swine herds with *L. pomona* bacterin should be recommended to livestock owners as a means to halt the spread of the disease.



Small Animal

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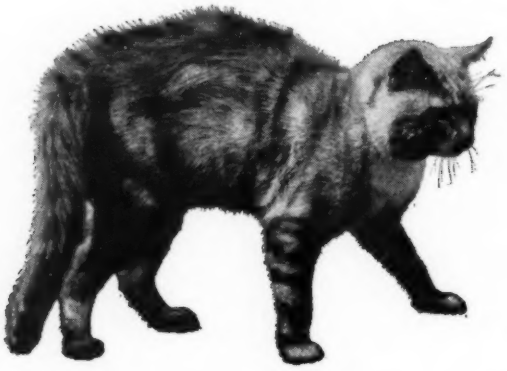

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Leptospirosis Of Pet Animals†

J. E. MOSIER, D.V.M., Manhattan, Kansas

THE occurence of leptospirosis in pet animals was first suspected in 1916 when Krumbien and Freiling reported on two persons who developed Weil's disease after exposure to a dog with jaundice. That the syndrome, then called infectious jaundice of dogs, was due to *Leptospira icterohemorrhagiae* was first established by Okel *et al.* in England in 1925. Dutch workers were the first to recognize *L. canicola* as an etiological agent in the dog in 1931. *L. canicola* was first recovered in the United States from the dog by Meyer *et al.* in 1937. Randall and Cooper (1943) were the first to recover *L. icterohemorrhagiae* from a dog in the United States.

Since 1939, several serological surveys have been conducted in different areas of this country in an attempt to determine the incidence of leptospirosis in the canine population. These surveys have established that *L. canicola* is the primary cause of leptospirosis in dogs. The incidence of *L. canicola* has varied from zero, as reported by Meyer working in Alabama in 1939, to 26.2% as reported by Newman in a survey conducted in Michigan in 1950. Incidence of *L. icterohemorrhagiae* has varied from zero as reported by Meyer working in Alabama and California in 1939 to 8% as reported by Raven in a survey conducted in Philadelphia in 1941. Other surveys made in this country have supported this preponderance of occurrence of *L. canicola* over *L. icterohemorrhagiae* in dogs. While the number of animals tested and the areas covered by these surveys are limited, results are sufficiently significant to illustrate the importance of leptospirosis as a disease producing agent among dogs in this country.

Incidence of leptospirosis in cats is unknown. Collier and Esseveld, working in Java following an outbreak of rice-field fever, reported 33% of cats tested serologically positive to *L. javanica.* Hemsley in England reported *L. canicola* infection among cats and mentions the serological evidence of *L. icterohemorrhagiae* among the feline population. Not having observed a known case of leptospirosis in the cat, my remarks will be limited to leptospirosis in the dog.

Clinical Canine Leptospirosis

While it is generally conceded that leptospirosis due to *L. icterohemorrhagiae* is more severe than that due to *L. canicola* both organisms are capable of producing a syndrome which may vary from a mild, relatively inapparent infection to a type that is rapid and fulminating. From the clinical standpoint, little emphasis is placed on absolute identification of the organism.

Five general clinical types of leptospirosis may be recognized according to severity of illness. It must be emphasized that the five types to be listed are not distinct entities and that considerable overlapping will occur. They are listed only to aid in clarifying the syndrome as observed in dogs. The first type, subclinical leptospirosis, is one that is rarely diagnosed. It produces a rather vague tran-

†Presented at the Interprofessional Symposium on Leptospirosis, Postgraduate Medical Study, University of Kansas Medical Center, Kansas City, Kansas, April 25, 1957.

sient illness and is probably most common, but due to the lack of adequate laboratory procedures for easy confirmation of diagnosis and relatively minor medical aspects of the disease, it is usually dismissed as an intestinal upset, chills, mild fever, or gastritis. The number of dogs that are serologically positive without a history of definite illness would support this observation.

The second classification may be referred to as a hemorrhagic type. It is characterized by rather violent onset accompanied by moderate to severe intestinal hemorrhage. Animals suffering from this type of disease probably will die unless treatment is prompt and intensive. It is the hemorrhagic type that is usually observed in dogs dying of the peracute form.

The third classification refers to the septicemic form of the disease accompanied with jaundice. This may occur as an extension of the hemorrhagic type. The only difference between the septicemic disease with jaundice and the hemorrhagic type is the degree of liver involvement. Jaundice may also occur in the later stages of more typical leptospirosis and whenever it occurs in small animals usually it is viewed with considerable concern. As the degree of jaundice increases rate of recovery decreases. Witter gives the incidence of jaundice as varying from 3 to 50% of the cases observed in any epizootic.

The fourth type is the classical textbook form of leptospirosis characterized by an acute infectious disease leading to nephritis and uremia. It is most typical of the average clinical case of leptospirosis.

The fifth or chronic type is difficult to diagnose. Because of the lowered vitality and resistence on part of the animal, secondary bacterial infection is common. This particular form of leptospirosis may be difficult to distinguish from other diseases, such as chronic bacterial infection, upper respiratory infections, and distemper of the dog. The finding of an elevated blood urea nitrogen (BUN) may suggest the possibility of leptospirosis in these cases. It must be emphasized again that these five types are not distinct entities and that considerable overlapping occurs. A combination of any of these may occur and complicate diagnosis.

Signs of Disease

Symptoms of typical leptospirosis of the dog vary with the stage of disease when the patient is presented for treatment. The septicemic stage, which occurs during the first three to seven days of the syndrome, is followed by the toxic stage. During the septicemic stage, the patient has a rather characteristic "tucked up" appearance of the abdomen. Lethargy and muscular temors are noted consistently. Muscular tenderness and stiffness causes the animal to move in a stilted fashion, palpation of the area over the kidneys is usually painful. The dog is reluctant to stand from the sitting position, will not jump over small barriers, and almost refuses to go up-stairs. Patients are ordinarily sensitive in the groin which is sometimes considered to be pathogomonic. The conjunctival and oral mucous membranes are congested, with petechial hemorrhages occurring in buccal membranes, pharynx and epiglottis.

There may be difficulty in swallowing due to pharyngitis. The cervical lymph glands may be swollen and a cough may be present. Occasionally vomiting accompanied by constipation or diarrhea are frequent observations of the owner and the rectal temperature will vary from 103 to 106 F. Pulse and respirations usually are increased and if an enema is given it may bring forth yellow or orange colored feces that are "putty-like" in consistency.

As the disease progresses and the organic effects of the infection become apparent, the toxic stage is entered. This occurs usually three or more days after onset of illness. Symptoms just described are more pronounced. Body temperature is usually normal to subnormal. Congestion of the mucous membranes becomes more intense and icterus may be evident. The areas of petechiation within the mouth become blanched and begin to ulcerate. Gum margins bleed when touched and the teeth may be coated with a brown, slimy mucus. Occasionally the tongue may become necrotic and slough although this usually occurs only in advanced cases. Vomiting and diarrhea are common and usually contain considerable bile. In the terminal stages, free blood may be found in the vomitus and feces. Rapid dehydration and emaciation result from gastroenteritis. Symptoms of nephrosis and uremia with typical fetid breath, occurs as a result of kidney damage. At this stage, the dog is showing evidence of severe emaciation, refuses to eat, vomiting is rather profuse, and anemia is pronounced. Fatal cases usually die within five to ten days of the first evidence of illness. A few acute cases

die in the septicemic stage as a result of profuse tissue hemorrhage.

Meningitis is reported as occurring in man but little nervous involvement has been reported as occurring in the dog. However, meningitis will be observed occasionally associated with *L. canicola* in the terminal stages. The occurrence of meningitis in these cases may complicate a rather characteristic picture of leptospirosis, making it difficult to distinguish clinically from distemper, toxoplasmosis, infectious hepatitis, et cetera. Incoordination with inability to stand, whining, hypersensitivity, paddling movements of the feet and legs are characteristic of leptospiral meningitis. If the patient survives the critical stages of illness, convalesence will depend on the degree of tissue destruction, especially in the kidneys and liver, and upon physiological balances that vary from patient to patient. Polyuria and polydypsia are usually noted and related to the degree of morphologic renal alterations.

Other signs of renal insufficiency are quite variable and may be mild or severe, intermittent or continuous, and of indefinite duration. In subacute and chronic cases, the insufficiency depends upon whether the renal function is compensated or decompensated. In the acute stage, the course is rapid and death may occur in three to 14 days. An interval of one to 2½ years may occur between onset of illness and death from uremia in chronic cases. Characteristic roughening on the crown of the nose is observed frequently in animals recovering from leptospirosis.

Clinical Laboratory Findings

In acute hemorrhagic and icteric types hemoconcentration occurs with an increased white blood cell count which may vary from 15,000 to 35,000 but in most instances is from 15,000 to 20,000. Increased sedimentation rates usually are noted. Urinalysis may reveal a high specific gravity with proteinuria, bile, casts, and red blood cells. In the toxic uremic stages, the blood picture is similar to the hemorrhagic type with the addition of increased urea nitrogen values which may sometimes be extremely high. The highest observed in our clinic has been 480 mg.%. Some of the blood electrolytes, especially phosphates, are increased and chlorides generally decreased. Anemia is a rather constant finding. If uremia is present, urinary changes such as low specific gravity, slight proteinuria with occasional tubular casts, are noted. These findings when associated with clinical observations may lend considerable support to the final diagnosis of leptospirosis. For more positive diagnosis blood and urine cultures of suspect animals, inoculation of susceptible laboratory animals, especially the hamsters, and the agglutination-lysis test may be utilized.

In closing, it may be stated that canine leptospirosis may be sporadic with a tendency for a rapidly developing enzootic appearing for short periods. Leptospirosis may occur throughout the year. The sex ratio reveals an incidence of approximately five males to one female, to quote Bloom's figures. The incubation period is estimated to range from five to 18 days with an average of nine days.

The clinical manifestations of canine leptospirosis are extremely variable. They may be absent, latent, subclinical, atypical, mild, or severe.

▾ ▾ ▾

Osteodystrophia

We received an inquiry a short time ago from a colleague in which he inquired about digital osteodystrophia in dogs. Our personal experience with the ailment is limited and based solely on clinical manifestations. Taken as a whole, the digital symptoms appear to be an evidence of demineralization which, when it occurs in a limited or rather minor general condition, is frequently unnoticed, but as the disease progresses at least one or two clinical evidences appear in the jaw and/or in the digits. It has been advanced that a difference in the nature of the bone and their Haversian systems is responsible for these localizations (it is known as "rubber jaw" in some countries).

Apparently, the demineralization is a sequel of chronic nephritis associated with phosphorus retention, however, though chronic nephritis is observed in the osteodystrophic changes it does not necessarily follow that chronic nephritis is always manifested clinically by the more or less extensive changes observed in the jaw and digits. Also as an etiological factor, a parathyroid hyperplasia is evident. It would appear that in these advanced evidences of the condition it is already so complicated and in such an advanced stage that prognosis is exceedingly grave. Such agents as minerals, cod liver oil, and direct sun exposure have been advocated.—*R. R. Dykstra, D.V.M.*

The Laboratory Diagnosis Of Leptospirosis†

HERBERT G. STOENNER, D.V.M., Hamilton, Montana*

THIS discussion will be confined to serologic methods used for the diagnosis of leptospirosis.

Technics

More methods probably have been devised for the laboratory diagnosis of leptospirosis than for the diagnosis of any other disease of man or animals. The first technic employed was the agglutination-lysis test described by Schüffner and Mochtar.[1] This test is tedious and time consuming and furthermore, cultures of leptospires must be maintained continuously to provide living antigen. Consequently, modifications have been introduced and other methods have been devised to simplify leptospiral serology. In some laboratories, formalin killed leptospiral suspensions are used, but agglutination must still be evaluated by darkfield examination of each serum dilution. To eliminate this time consuming task, some workers have used aggluination tubes of various shapes and sizes in which reactions could be read by gross visual examination. The complement-fixation system has been used in many laboratories and antigens for use in this system have been prepared by various methods.[2,3,4] Recently, a combination plate and capillary-tube test and several plate antigens were developed.[5,6,7]

Advantages and limitations are inherent in each technic. The agglutination-lysis test is specific, extremely sensitive and it can detect antibodies in serums of man or animals for an extended period after infection. However, as mentioned previously, this test is time consuming and cultures of leptospires must be maintained as a source of antigens. While the use of formalin killed antigens reduces the health hazard to personnel, the unpredictable stability of killed leptospires in their original culture medium may cause erroneous results if proper controls are not included in the test system. This disadvantage also applies to the macroscopic tube-agglutination test in which reactions are read without the use of darkfield microscopy. The complement-fixation test is more complex than an agglutination system but some workers who routinely use the former for diagnosis of other diseases advantageously apply the complement-fixation system to leptospiral serology. Since antibodies detectable by this test disappear from serums of a high percentage of hosts within several months postinfection, the rather brief retrospect of the complement fixation test is a major limitation. The combination plate and capillary-tube test is extremely simple and rapid, and it can detect antibodies in retrospect for a period intermediate between retrospects of the agglutination-lysis test and the complement-fixation test. Satisfactory plate antigens are difficult to prepare. However, since commercial firms have made antigens from the major serotypes available, this disadvantage has been overcome.

TABLE 1. The Effect of Antigens of Varying Cell Concentrations on Titers of 20 Bovine Serums Examined by the Agglutination-lysis test.*

Cell content	No. of serums positive at indicated titer. 1:250	1:1,250	1:6,250	1:31,250
6.5 x 10^8/ml.	7	12	1	....
3.25 x 10^8/ml.	3	11	6	....
1.625 x 10^8/ml.	2	7	11	....
8.125 x 10^7/ml.	....	6	13	1

*Stoenner, H. G., Proceedings, Am. Vet. Med. Assn., 92nd annual meeting, Minneapolis, Minn., Aug. 15-18, 1955, pp. 172-176.

Much confusion has been created because many technics are employed and because results of tests by one method may not be similar to those obtained by another. For example, the time after onset that serums are obtained would influence correlation between the complement-fixation test and other technics. Furthermore, few workers use exactly the same methods and such modifications undoubtedly affect results.

Since the agglutination-lysis test is used in many laboratories, an illustration of the effect of variables on results obtained by this technic seems warranted. One variable, most difficult

†Presented at the Interprofessional Symposium on Leptospirosis, Postgraduate Medical Study, University of Kansas Medical Center, Kansas City, Kansas, April 25, 1957.

*From the U. S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, National Institute of Allergy and Infectious Diseases, Rocky Mountain Laboratory, Hamilton, Montana.

TABLE 2. The Effect of Varying Serial Dilutions of Serum on Titers of 20 Bovine Serums Examined by the Agglutination-lysis test.* **

Serial dilution	Minimum titer	Geometric mean titer	Maximum titer
Twofold	1:320	1:1,196	1:2,560
Fivefold	1:250	1:1,950	1:6,250
Tenfold	1:1,000	1:5,012	1:10,000

*Leptospiral content of antigen adjusted to contain about 2.5 x 8 cells per ml.

**Stoenner, H. G., Proceedings, Am. Vet. Med. Assn., 92nd annual meeting, Minneapolis, Minn., Aug. 15-18, 1955, pp. 172-176.

to control in this test, is the cell content of the antigen. When the leptospiral content of the antigen is decreased, resulting titers of serums are correspondingly elevated (table 1). Few workers employ the same system of diluting serums for tests. When the same pipette is used for succeeding dilutions, titers obtained when serums are tested in decimal dilutions are significantly higher than those obtained when two-fold serial dilutions of serums are tested (table 2). When two variables that tend to elevate titers are combined in a test, results are grossly different from those obtained when two variables that depress titers are combined (table 3). These illustrations may explain discrepancies in results obtained even by workers employing the same method.

Selection of Samples

The problem of establishing a diagnosis of leptospirosis in the practice of human medicine differs from that encountered in veterinary medicine. Since most cases in man are sporadic, the physician is concerned only with the individual patient. Because a diagnosis can not be confirmed by serologic tests until early convalescence, therapy can not be guided by serologic findings. Although establishing the etiology of a febrile illness is important *per se*, the physician also should utilize laboratory findings to confirm his clinical impressions and thereby improve his diagnostic acumen. The first blood specimen should be taken during the acute phase, preferably before antibiotics have been administered. This sample should be utilized for the isolation of leptospires and for a base line to determine any future rise in antibody titer. In some instances patients with meningitis may possess antibodies at the time of initial examination, but usually the physician has adequate opportunity to secure a first serum free of antibodies. Two to three weeks after onset, a second specimen should be obtained so that a rise in antibody titer during convalescence can be demonstrated.

Since leptospirosis of livestock usually is a herd problem, the attending veterinarian may have the opportunity to avert further losses if a diagnosis can be established during the early epizootic period. This can be done in instances when veterinary consultation is requested after signs of leptospirosis, such as abortions and febrile agalactia, are first noted. Blood specimens obtained from cattle at the time of abortion or from those ill ten days to two weeks previously usually possess antibodies in high titer, whereas those obtained at the time of febrile agalactia are free of antibodies. Often clinical signs in affected dairy cattle are sufficiently typical to warrant prompt initiation of control measures without waiting for laboratory confirmation. Particular reference is made to cases of acute agalactia, characterized by high fever and thickened and blood-tinged milk. Ideally, a diagnosis of leptospirosis should be based on a rise in antibody titer; however, if further losses are to be prevented by immunization, a diagnosis must be made early and control measures should be instituted promptly. Ordinarily, an epizootic of leptospirosis has progressed to some extent before the disease is suspected. Frequently early infections are inapparent and clinical signs do not appear until later in the epizootic. At the time veterinary assistance usually is requested, 25 to 50% of a herd of cattle or swine may possess antibodies in high titer.

Interpretation of Results

When a herd of swine or cattle is found to contain serologically positive animals, the veterinarian must decide whether results of tests reflect recent infections or residual levels of antibody remaining from infections experienced several years previously. In recently

TABLE 3. The Effect of Combinations of 2 Variables on Agglutination-lysis Titers of 20 Bovine Serums that Possessed a High Level of Antibody.*

Serial dilution	Antigen cell concentration	Minimum titer	Geometric mean titer	Maximum titer
Twofold	6.5 x 10^8/ml.	1:10,240	1:31,055	1:81,920
Tenfold	8.125 x 10^7/ml.	1:100,000	1:1,259,000	1:10,000,000

*Stoenner, H. G., Proceedings, Am. Vet. Med. Assn., 92nd annual meeting, Minneapolis, Minn., Aug. 15-18, 1955, pp. 172-176.

TABLE 4. Comparison of Serologic Findings in Herds of Cattle Recently Infected with *L. pomona* with Findings in Herds with Residual Serological Evidence of Past Infection.**

Titer of serum			Distribution of serums from each herd at indicated titers.											
Examined by:			Recently infected herds						Herds with residual antibody from previous infections					
			A		B		C		D		E			
CF*	CT	AL	CT	AL	CT	AL	CT	AL	CT	AL	CF	CT	AL	
Neg. (<1:16)	Neg. (<1:40)	Neg. (<1:100)	119	119	8	8	21	19	35	25	95	74	49	
1:16	1:40	1:100	2		4		18	7	49	31	23	51	19	
		1:500		2		1		12		28			40	
1:32	1:160	1:5,000		3	3	4	35	16	9	7	30	33	36	
		1:50,000		2		1		25		5			33	
1:64	1:640	1:500,000	6	1	19	20	85	80	8	5	37	27	8	
Totals			127		34		159		101		185			

*Only serums from herd E. were tested by the complement-fixation test, performed by the Serology Section, Rocky Mountain Laboratory, Hamilton, Montana.
CF — Complement-Fixation Test CT — Capillary-Tube Test AL — Agglutination-Lysis Test
**Stoenner, H. G., Proceedings, Am. Vet. Med. Assn., 92nd annual meeting, Minneapolis, Minn., Aug. 15-18, 1956, pp. 172-176.

infected herds, the majority of serologically positive animals possess high titers, whereas in herds of cattle that had leptospirosis several years previously, a greater proportion of serologically positive animals possess low titers (table 4).

Most investigators consider titers of 1:100 to 1:500 or greater obtained with the agglutination-lysis test as significant, *i. e.*, evidence of past experience with leptospires. Although bovine serums occasionally possess nonspecific agglutinins at the lower level[8] this interpretation can be applied practically when serums of man or domestic animals are examined by this technic. Bovine serums occasionally possess nonspecific agglutinins at a titer of 1:40 with the plate and capillary-tube test; hence, a herd of cattle may be considered free of leptospirosis if none of the serums have titers greater than 1:40. However, in infected herds, such titers more likely reflect true antibody than nonspecific agglutinins. Since such nonspecific agglutinins have not been encountered in serums of man or other animals, a titer of 1:40 or greater with the plate or capillary-tube test is considered significant.

Finally, paraspecific reactions should be considered. This reaction may be defined as the development of predominant agglutinins against a serotype other than the one infecting the host. Such reactions have been noted in studies of both human and bovine leptospirosis. For example,, *Leptospira pomona* has been isolated from herds of cattle that possess antibodies principally against *L. sejroe*.[9] Therefore, a diagnosis of infection with a particular serotype can not be based on serologic findings alone. The Leptospira should be isolated and its antigenic composition should be characterized.

REFERENCES

1. Schüffner, W. and Mochtar, A., Versuche zur Aufteilung von Leptospirenstämen mit einleitenden BemerKungen üeber den Verlauf von Agglutination and lysis. *Centbl. f. Bakt. I.* Abt. Orig., 101:405, 1927. Abstract: *Trop. Dis. Bul.*, 24:714, 1927.
2. Gaehtgens, W., Beitrag zur Serodiagnosis der Weilschen Krankheit. *Klin. Wchnschr.*, 12:697, 1938. Abstract: *Trop. Dis. Bul.*, 30:724, 1933.
3. Randall, R., Wetmore, P. W., and Warner, A. P. Jr., Sonic-vibrated Leptospirae as Antigens in the Complement Fixation Test for the Diagnosis of Leptospirosis. *Jour. Lab. and Clin. Med.*, 34:1411, 1949.
4. York, C. J., A Complement-Fixation Test for Leptospirosis in Cattle. *Am. Jour. Vet. Res.*, 13:117, 1952.
5. Stonenner, H. G., Application of the Capillary-tube Test and a Newly Developed Plate Test to the Serodiagnosis of Bovine Leptospirosis. *Am. Jour. Vet. Res.*, 15:434, 1954.
6. Hoag, W. G., Gochenour, W. S., and Yager, R. H., Leptospiral Macroscopic Agglutinating Antigens. *Proc. Soc. Exp. Biol. and Med.*, 83:490, 1953.
7. Bryan, H. S., Studies on Leptospirosis in Domestic Animals: VII A Rapid Plate Agglutination Test for *Leptospira pomona*. *Vet. Med.*, 52:111, 1957.
8. Stoenner, H. G., Crews, F. W., Crouse, A. E., Taschner, L. E., Johnson, C. E. and Wohleb, J., The Epizootiology of Bovine Leptospirosis in Washington. *Jour. Am. Vet. Med. Assn.*, 129:251, 1956.
9. Galton, M. M., Acree, J. A., Lewis, A. and Prather, E. C., Leptospirosis in Domestic Animals in Florida with Reference to Cattle. *Jour. Am. Vet. Med. Assn.*, 128:87, 1956.

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New Tuberculosis Vaccine

A new tuberculosis vaccine developed by Parke-Davis and Co., Detroit, is claimed superior to BCG as a practical immunizing agent in man. The product is prepared from a human strain of organisms and retains its antigenic properties during comparative long periods.

Present work with the new vaccine is said to be a phase of the experimental trials.

The Pathology of Leptospirosis In Animals†

M. J. TWIEHAUS,* D.V.M., M.S., Manhattan, Kansas

LEPTOSPIROSIS, as has been brought out in other papers, is an infectious disease of animals and man caused by one of the spirochetal microorganisms of the genus, Leptospira. The disease is apparently widespread, and majority of cases occur in animals as an inapparent infection. Animals may also act as reservoirs for the disease in man. The species most commonly found in the United States in cattle, swine, and horses is *L. pomona*.[1] In dogs, *L. canicola* is most frequently isolated, but *L. icterohaemorrhagiae* has also been found in some cases.[2] Because of the time limitation, I will discuss only the pathology observed in dogs and cattle.

Canine Leptospirosis

Gross changes observed in dogs may vary, depending upon whether the disease is acute or subacute. Dehydration in infected animals is marked, and icterus is usually apparent. Sclera and conjunctiva may also reveal marked congestion and icterus. Hemorrhages (petechial, ecchymotic) of various organs and tissues are probably the most outstanding finding on necropsy. Similar findings have been reported by other workers.[2,3] The oral mucosa may be studded with ecchymotic hemorrhages, particularly along the gum line. (See fig. 1). These areas of hemorrhage may undergo ulceration if death does not occur too rapidly. The membranes of the mouth may be coated with a slime or mucus that has a disagreeable odor. Nasal passages are congested, and the lumen may contain mucus tinged with blood. The pleura of the lungs frequently is covered with a few or numerous petechial or ecchymotic hemorrhages.[3,4] The lumen of the stomach may contain free blood, and the mucosa may exhibit petechiation or extensive hemorrhages. Intestine is less frequently involved, although petechia may be found on the mucosal and/or serosal surface in some cases. Occasionally blood mixed with the feces may be observed in the lumen. If blood is not present in the intestinal lumen, feces usually are highly colored (yellow to orange) and frequently pasty. Tonsils are congested and usually dark red. Kidney may be slightly swollen and a few petechia observed. Grossly, the liver and other organs may reveal some changes, but these are usually not marked. Microscopic findings of the kidney and liver are primarily degenerative in nature. Changes in the kidney are confined mainly to the tubular epithelium and interstitial tissue. Glomeruli, in most cases, are not involved. The epithelium of the tubules may reveal cloudy swelling, vacuolization, and necrosis. Regenerating epithelium may be observed in various stages. The lumen of the tubules usually contains some cellular debris. Interstitial tissue may, in some cases, be infiltrated with various inflammatory cells — lymphocytes, plasma cells, macrophages, and neutrophils. The liver may also reveal evi-

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Fig. 1. Leptospirosis in a dog. Note ecchymotic hemorrhage (arrow) on oral mucosa.

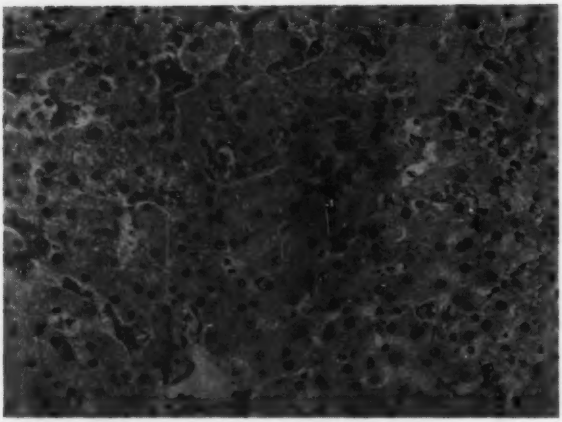

Fig. 2. Leptospirosis in a dog. Note disruption of liver cord cells.

Courtesy of the Animal Disease and Parasite Division, Agricultural Research Service.

dence of degenerative changes. The normal cord arrangement in many cases is distorted. (See fig. 2). Blood pigments may also be observed scattered throughout liver cord cells.

Bovine Leptospirosis

Gross pathology of acute leptospirosis may be similar to that described in dogs. The acute type is usually characterized by icterus and anemia of the mucous membranes. In many cases in a milking animal, the udder may be flaccid and the milk discolored or flaked with blood. If pregnant animals are affected, abortions may occur 12 to 14 days after infection. Hemoglobinuria and hemoglobinemia are frequent findings in the acute type.[8] (See fig. 3). Small hemorrhages may be found scattered throughout the tissues.

The kidneys may be slightly congested and somewhat swollen and contain areas of blood pigment on the surface resembling hemorrhages. (See fig. 4). In the subacute type, the surface of the kidney may be spotted with small or minute white to gray foci.[5,6] Focal lesions in the kidney have been observed mostly in younger animals or calves. Hadlow and Stonner[7] reported these findings in adult animals. I would also like to mention that similar lesions could, no doubt, be caused by other agents or disease. The liver may be mottled and slightly swollen. Some workers reported a yellowish to orange discoloration of the liver.[9] In many cases, gross changes are not observed in this organ. The hepatic nodes are usually swollen and edematous. Mucosa of the abomasum usually exhibits hemorrhagic foci and ulcerations. Lungs are not involved and in most cases, only areas of emphysema and edema are observed. This finding is pronounced in cases of hemoglobinemia. The microscopic changes are more consistent than gross findings.

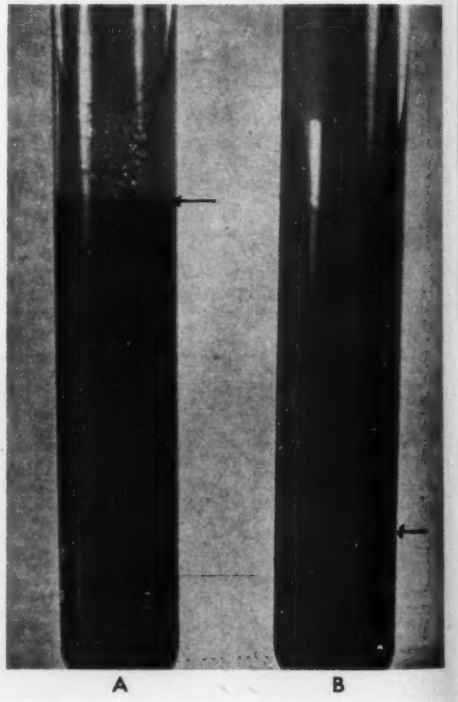

Fig. 3. Citrated blood tubes. A. Normal. B. Anemia and hemoglobinemia (note discoloration of serum above cells).

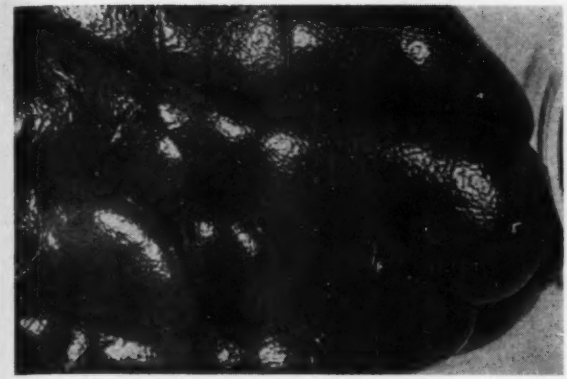

Fig. 4. Bovine kidney showing brownish foci resembling hemorrhage.

The most consistent finding in the kidneys is a focal interstitial nephritis. Tubular epithelium of the convoluted tubules reveal various stages of degeneration and also regeneration. These involved tubules are usually surrounded by cellular infiltration (lymphocytes, plasma cells, etc.). Casts also are observed frequently in the tubules. The glomeruli generally are spared.

In closing this discussion, I would like to emphasize for the benefit of practicing veterinarians that with varied clinical symptoms and gross pathological findings, it is essential that laboratory tests be conducted before establishing a diagnosis of the problem that is presented in the field.

REFERENCES

1. Gochenour, W. S. Jr., Yager, R. H. and Wetmore, P. W., Antigenic Similarity of Bovine Strains of Leptospirae (United States) and *Leptospira pomona*. *Proc. Soc. Exp. Biol. Med.*, 74:199, 1950.

2. Bloom, F. Canine Leptospirosis., Symposium on the Leptospirosis Medical Science Publication, No. 1, Dec., 1952.

3. Monlux, W. S., The Pathology of Canine Leptospirosis. *Cornell Vet.*, 38:199, 1948.

4. Meyers, K. F., Stewart-Anderson, B., and Eddie, B., Canine Leptospirosis in the United States. *Jour. Am. Vet. Med. Assn.*, 95:710, 1939.

5. Cordy, D. R., and Jasper, D. E., The Pathology on Acute Hemolytic Anemia of Cattle in California Associated with Leptospira. *Jour. Am. Vet. Med. Assn.*, 120:175, 1952.

6. Reinhard, Karl R., Bovine Leptospirosis. Medical Science Publication, No. 1, Army Medical Service Graduate School, Walter Reed Army Medical Center.

7. Hadlow, W. J., Stonner, Herbert G., Histopathological Findings in Cows Naturally Infected with *Leptospira Pomona*. *Am. Jour. Vet. Res.*, 16:45, 1955.

8. Reinhard, Karl R., Tierney, William F., and Roberts, Stephen J., A Study of Two Enzootic Occurrences of Bovine Leptospirosis. *Cornell Vet.*, 40:148, 1950.

9. Mathews, Frank P., A Contagious Disease of Cattle Associated with Leptospirosis. *Am. Jour. Vet. Res.*, 7:78, 1946.

Treatment of Canine Pyometra

Cowie and Muir discuss informatively, The Use of Quinine in the Treatment of Pyometra in the Bitch (*The Veterinary Record*, Aug. 1957). In developing their presentation of the subject they bring out that surgical intervention is frequently impractical, that the use of hormones may disturb further the endocrine balance, and that quinine (we assume the sulfate) has both tonic and ecbolic therapeutic action and that it sometimes is used by human medical practitioners to contract the uterus so that contained contents, if any, are evacuated. The dose varies initially depending upon the size of the bitch, from 2.5 to 10 gr. daily reduced by half this quantity each day. Treatment to be continued for seven to ten days, and if there is a recurrence of the condition, another similar course of medication is advised. The authors report that 52 cases have been treated in this manner with excellent results.

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Leptospirosis Isolated from Ticks

Epidemiologists will now be required to take a closer look at outbreaks of leptospirosis when searching for source of infection. Whereas direct contact exposure or ingestion of contaminated feed or drinking water are usually given as infection source, insects or acarid pests may be vectors responsible.

Researchers report[7] isolation of two strains of pathogenic leptospires of the *L. grippotyphosa* serotype from the tick *Dermacentor marginatus* collected in their natural habitat.

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[7]Krepkogorskaia, T. A., and Rementsora, M. M., The Isolation of Strains of Leptospires from the Tick *Dermacentor marginatus* from Cattle. *Jour. Micro., Epid., and Immunolio.*, 28:251, 1957.

Treatment Of Leptospirosis In Animals†

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DOCTOR Stockard very ably covered the use of antibiotics treatment of leptospirosis. I should say that not having observed our cases from a standpoint of laboratory procedures we have some difficulty in evaluating the efficacy of various antibiotics. For some time we have believed that these agents were successful in animals, particularly in the early acute stages, and have always made it a practice to administer them when patients are presented. I recall a good many failures bearing out what had been said on the subject. We also have had some favorable experiences which may have been coincidence. I would like to outline our standard treatment in small animals without giving detailed individual case results.

Medical Management of Infection in Small Animals

Generally, the treatment of leptospirosis in small animals is practically the same as it is for any acutely or chronically ill patient, and depends upon the stage of leptospirosis that might be present. Treatment is most effective in the early stages and is of little or no value in cases with irreversible renal lesions. In the septicemic stage of the acute syndrome, causative organisms are circulating in the blood stream. In its passage, it produces damage to tissues which may be due in part to its mechanical effects, and in part to metabolic products of the organism. Furthermore, it is quite possible that leptospires liberate a powerful exotoxin. Ferguson and coworkers at Ohio postulate the liberation of a toxin when large numbers of leptospires are destroyed by antibiotics.

To combat the organism, antibiotics have been used. For several years we have administered 300,000 units of procaine penicillin and 0.5 gm. streptomycin twice daily to dogs weighing 25 to 50 lb. At the same time potassium G penicillin administered subcutaneously or intravenously every six hours, is prescribed at the rate of 200,000 units per dose to be continued until body temperature returns to normal. It is difficult to say whether the antibiotics accomplish resolution of the acute infection. We have always believed it to be worthy of trial, and have prescribed the treatment persistently. Penicillin has been represented as being effective against leptospiremia by various workers, but not against leptospiruria. It has been suggested that 80% of the penicillin excreted by the urine is excreted by way of the distal portion of the urinary tubules. Since leptospires occupy positions in the proximal convulated tubules this may explain why penicillin is not effective in clearing leptospiruria.

Hyperimmune serum is beneficial particularly in the early septicemic stage but of little or no value in those patients that are in the toxic stage of the disease. This is understandable because it has been fairly well established that when the toxic stage develops leptospires have disappeared from the blood stream and that normal body defense mechanism is functioning.

Dietary Regimen

In addition to antibiotics we ordinarily administer glucose orally if possible. A high carbohydrate diet is prescribed and a high protein intake is recommended if there is no evidence of renal lesions. If the patient is unable to retain food, then 5% glucose solution intravenously is prescribed, particularly to provide a source of energy and to maintain body stores of glycogen. Maintaining an adequate supply of glucose tends to prevent acidosis and has a sparing effect on protein catabolism. If vomiting occurs, glucose and saline may be given parenterally to supply energy and to combat hypochloremia.

Fever that is associated with the septicemic stage will cause a rapid depletion of the vitamin reserves. These should be replaced with particular attention to the water soluble B complex. This reference to the B complex is made because these elements are the ones most likely to be depleted, and because of

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†Presented at the Interprofessional Symposium on Leptospirosis, Postgraduate Medical Study, Kansas University Medical Center, Kansas City, Kans., April 25, 1957.

*Professor of Small Animal Medicine and Surgery, School of Veterinary Medicine, Kansas State College.

their importance in carbohydrate metabolism. If hemorrhage is severe, blood transfusions are indicated. Freshly drawn blood is employed rather than stored blood, which eliminates the possibility of adding excess potassium that might already be present. In case of suspected liver damage, vitamin K is administered to aid in preventing possible hypoprothrombinemia. The diet should consist of foods rich in carbohydrates and high quality protein, provided the patient is able to utilize oral feeding. Should evidence of kidney damage be present, protein intake should be restricted. This is particularly true as signs of renal insufficiency develop in the toxic stages.

An increase in the specific gravity of the urine, albumiuria, and the presence of hyaline and granular casts as a result of the kidney inflammation are the first indications of kidney damage. Since the renal pathology is the forerunner of uremia the use of protein either as a food or as a hydrolysate should be reduced greatly to prevent the buildup of nonprotein nitrogenous constituents in the blood.

Supportive Therapy

The development of diarrhea — and it frequently develops — may call for the substitution of lactated Ringer's solution or other electrolyte solutions in the place of saline as a means of combating acidosis. Intestinal protectants and astringents may be given, although, they seem to be relatively ineffective. With the appearance of uremia other factors must be considered. In most cases this is of gradual occurrence and according to Sodeman, develops when 60% of normal function is lost. Retention of phosphates, possibly phenols and potassium, with accompanying acidosis are associated with uremia.

Administration of calcium will overcome the calcium deficit due to the retention of phosphates as well as serving somewhat as an antagonist to potassium, thereby preventing cardiac embarrassment due to high potassium levels. Oral administration of aluminum hydroxdide will tend to reduce increased phosphate levels by causing fecal excretion of insoluble aluminum phosphate, thus preventing the absorption of more phosphate. Maintaining additional fluid intake with 5% glucose plus sodium chloride, sodium bicarbonate or lactated Ringer's solution is essential in the treatment of uremia. The use of desoxycorticosterone acetate to hasten elimination of urea, endogenous creatinine and potassium may be of benefit. Ott *et al.* at Washington State College, reported on their observation in one of the recent issues of VETERINARY MEDICINE. If used with adequate fluid therapy desoxycorticosterone may produce a rather dramatic drop in blood urea nitrogen levels of uremia. The dosage recommended is 2.5 mg. on alternate days for three doses or in mild cases 5 mg. as a single dose intramuscularly. For uremic dogs with severe stomatitis, the mouth should be flushed with sodium acid phosphate to counteract ammonia being released by the action of bacterial urases on the urea in saliva. Should recovery occur, the convalesence should be closely supervised. The most persistent lesion is that of chronic interstitial nephritis with accompanying polydypsia and polyuria.

Recurrent digestive disorders can be expected. Varying degrees of skin pathology, characterized by a dryness and pruritus are not uncommon. Most of the cases in which uremia has occurred must be maintained on a life-long diet of low quantity, high quality protein. The use of milk, milk products, eggs, oatmeal, cream of wheat, limited meat and adequate fat is a good dietary regime. The commercial prescription diet (K/D®) is excellent. A high vitamin intake, plus the use of cobalt and iron to combat anemia associated with uremia is beneficial. Feeding two or three times daily in limited amounts is preferable to once-a-day feeding.

Therapy in Large Animals

In larger animals, such as cattle and swine the treatment of leptospirosis is essentially the same as in dogs. However, the economic factor will have considerable bearing on the supportive therapy and how extensively it is employed. The primary aim of treatment is to preserve the life of the animal in the acute stages and to prevent or treat carriers of Leptospira. Considerable work has been done to determine methods of eliminating the carrier state. Streptomycin (5 mg. per lb.) given twice daily for three days, has been reported as effective by Ringer and others. Marshall reports 86% of the swine treated with oxytetracycline daily (5 mg. per lb.) for five days were cleared of leptospiruria. Baker *et al.* reported oxytetracycline fed at the rate of 500 to 1,000 gm. per ton of feed for 14 days eliminated the carrier state in 94 of 100 pigs. Howorth used tetracycline (3 mg. per lb.) intramuscularly for three days or chlortetracycline (200 mg. per lb. of feed), free choice for 14 days with good success. The use of

(Continued on page 552)

Leptospirosis: Infections In Man†

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Baltimore, Maryland

IN 1883 Landouzy and, three years later, Weil[1] described several human cases of leptospirosis. These were characterized by fever, hemorrhagic phenomena, hepatic, renal, and vascular decompensation, and a high fatality rate. Weil was credited with the first description of this disease which now bears his name. In 1915, Inada[2] isolated the etiologic agent, a spirochete, later named a leptospire by Noguchi.[3]

Improved bacteriologic research methods have since revealed many immunologically distinct leptospires to be pathogenic for man and a host of other animals. Many of these organisms are adapted in nature to unique epidemiologic patterns and produce highly variable clinical features in animals they infect. If all forms of the disease are to be properly identified, physicians must now recognize both the common and the unusual clinical features, as well as the environmental hazards which channel the infection to man.

The present paper will describe the clinical manifestations of classic Weil's disease, milder forms of leptospirosis observed in a tropical environment, and the varieties known to be present in North America.

Classic Weil's Disease
(Leptospira icterohemorrhagiae)

After an incubation period of four to 19 days, the disease begins abruptly. Rigor often is the first symptom, followed quickly by fever which then continues between 102 and 104 F. for about eight days and falls by lysis. Onset is followed by a rapidly developing symptom complex which includes prostration, severe, unrelenting headache, anorexia, and myalgia. Objective evidence of muscle tenderness is a characteristic clinical feature. Arthralgia may be intense. Nausea, vomiting, and diarrhea are frequently present and often are severe. In leptospirosis, mental confusion may occur earlier than in other infectious diseases.

Conjunctival injection without increased lacrimation is universally present, appears early, and persists for several days. Other ocular manifestations during the acute illness include hemorrhagic lesions in the retina, temporary and permanent oculomotor paresis, optic neuritis, and papilledema. Optic atrophy rarely develops. Leptospiral uveitis is the most constant complication and becomes evident two weeks to a year after the initial illness. In general, the prognosis is good for complete recovery of normal motor and visual functions.

Petechiae, subconjunctival hemorrhages, and profuse bleeding from the gastrointestinal tract do occur. An exanthem similar in appearance to that of rubella or scarlatina is not uncommon.

Death may sometimes result from severe peripheral vascular decompensation comparable to that observed in the rickettsial diseases. Myocarditis may impair the circulatory status even further.

Icterus, when present, usually appears at the end of the first week simultaneously with defervescence. It may intensify rapidly and persist for a month or more. Fatalities occur among the jaundiced, but intensity of icterus is not necessarily of prognostic significance. Hepatomegaly develops in the jaundiced but splenomegaly is seldom demonstrated.

Disturbed renal function is characteristic of Weil's disease. Only minimal proteinuria may be noted when the illness is mild, but in the seriously ill proteinuria is often heavy. Early in the second week of disease oliguria or anuria may appear. As in other conditions where urinary output is suppressed, severe azotemia and electrolyte imbalance develop. Fatalities often result from this serious complication. A sudden diuresis is considered a favorable omen. Permanent renal damage occurs rarely.

Findings referable to the central nervous system may dominate the clinical picture. Nuchal rigidity can be marked. Spinal fluid pressure is sometimes elevated while microscopic examination reveals a lymphocytic

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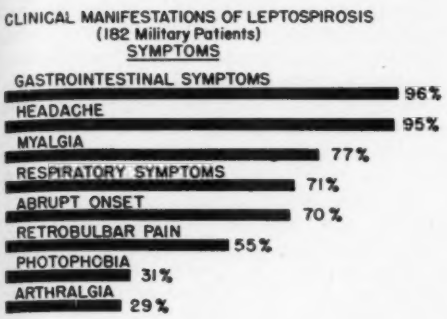
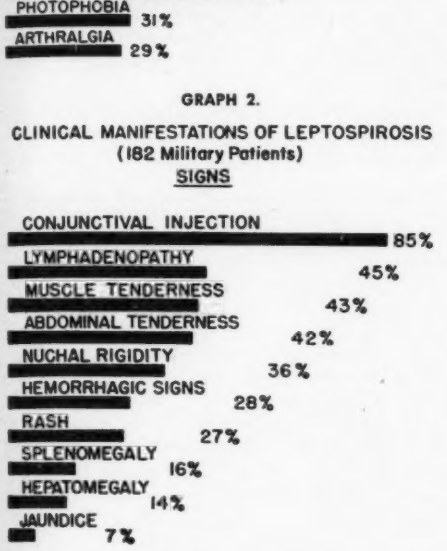
**Theodore E. Woodward, M.D., Professor, Department of Medicine, University of Maryland School of Medicine.

GRAPH 1.



GRAPH 2.



pleocytosis. Neuritis occasionally complicates the convalescence but usually the meningitis subsides uneventfully.

Examination of the peripheral blood usually reveals a leukocytosis with a preponderance of neutrophils. A hypochromic anemia is frequently noted.

Fatalities occur in approximately 30% of the jaundiced or in patients classified as severely ill. Occasionally death may ensue during the early stages of the disease as a result of vascular collapse or hemorrhage from the gastrointestinal tract. Usually the patient succumbs in the second week of illness from uremia. The controlling features therefore, are stability of the renal, hepatic, and vascular systems.

Mild Cases

Less severe forms of leptospirosis are prevalent in Malaya, where this diagnosis was confirmed in 244 of 852 febrile illnesses investigated in 1954 and 1955.[4] Leptospires isolated from the blood in 90 cases were subsequently identified. These represented 12 of the 20 serogroups recognized in the classification proposed by Wolff and Broom. Organisms of the icterohemorrhagiae and bataviae serogroups are usually responsible for severe Weil's disease and were isolated from six and ten cases, respectively in this study. The remaining strains usually produce milder illness[5] and did so in Malaya, as evidenced by the low mortality rate of 0.8%.

Clinical manifestations presented by these patients consisted of an acute febrile phase lasting about eight days and a convalescent phase of approximately two weeks' duration. Onset, abrupt in 70% of cases, was often marked by rigor. Shortly thereafter, fever, malaise, anorexia, headache, myalgia, and retro-orbital pain developed rapidly.

Anorexia and nausea occurred in 96% of the patients. Eighty-five per cent experienced emesis at least once during the febrile period, and many had almost continuous vomiting or retching. Mild diarrhea rarely occurred and except for these few instances, bowel function was undisturbed. During the febrile phase, headache and retro-orbital pain were continuous. Intensity of these symptoms varied in proportion to fever. Subjective myalgia was generalized and most severe in the calf, abdominal, pectoral, and cervical muscle groups. Cough, present in half of the patients, was productive in 50% of those with this complaint. Hemoptysis occurred in 60% of the cases with a productive cough, and was severe in two instances. A few patients complained of dyspnea, chest pain, coryza, and sore throat, but these did not constitute prominent features of the illness. Visual disturbances were never detected and photophobia was unusual.

Physical signs coincided with those usually observed in leptospirosis. Injection of the conjunctivae was present in 85% of the cases and appeared within 24 hours after onset. Its intensity as graded by the physician varied from 1 plus to 4 plus, the majority being graded 4 plus. Generalized lymphadenopathy was detected in half the patients, but enlargement of the nodes was less than is ordinarily observed in infectious mononucleosis, scrub typhus, or dengue. Objective evidence of muscular tenderness was demonstrated in 43% of the cases. This finding created difficulty in evaluating the significance of pain, particularly over the abdomen, costovertebral angles, and

neck. Appendectomy was performed unnecessarily in one instance. Examination of spinal fluid was performed in ten patients who had marked stiffness of the neck. Of these, six revealed lymphocytic pleocytosis ranging from 40 to 400 cells per cubic millimeter.

Hemorrhagic signs appeared from the fourth to eight days of disease and included the following, in decreasing order of frequency: Hemoptysis, hematemesis, epistaxis, petechiae, subconjunctival hemorrhages, melena, hematuria, ecchymoses, and submucosal hemorrhages in the pharynx. Abnormal bleeding was observed in patients infected by all serogroups except javanica, pomona, and sentoti. Bleeding was severe in two patients with hemoptysis, one of whom died on the fourth day after onset. *L. australis* B was isolated from the fatal case. Cough and signs of pulmonary congestion prompted roentgen examination of the chest in 42 cases. Abnormalities varying from slightly increased vascularity to small localized areas of consolidation were revealed on the films in 11 cases. Of these, six presented physical signs and roentgen evidence of pneumonia. In one instance, these findings dominated the clinical course. This patient's blood yielded *L. grippotyphosa* in culture. Other leptospires identified with clinical findings of pneumonia were from the pyrogenes, canicola, and schuffneri serogroups.

Skin eruptions, observed in one fourth of the group, appeared between the fourth and eight days of disease and persisted from a few hours to several days. These lesions consisted of either small macules or maculopapules, and were distributed over the head and neck, trunk, and upper extremities. Lesions resembling the rose spots identified with typhoid fever were seen in a few patients on the upper extremities, chest, and abdomen.

Splenomegaly and hepatomegaly were unusual, occurring in only 15% of the cases. Icterus detected by inspection alone was rare.

The total leukocyte count was usually normal, but leukocytosis and leukopenia did occur. Neutrophilia was noted in 80% of the patients during the febrile period.

Qualitative proteinuria, casts, and increased cellular elements were demonstrated at some time during the febrile phase in 80% of leptospirosis patients. Oliguria and mild azotemia developed in only 27 cases and never persisted longer than three days.

Liver function was evaluated serially by means of the van den Bergh reaction, total and fractional protein determination, and Kunkel's flocculation test. Liver function, as evaluated by these tests, was disturbed in two thirds of the patients. Elevations of total bilirubin values appeared early and rapidly returned to normal with defervescence. Abnormalities in the albumin-globulin ratios and Kunkel's test developed at the beginning of convalescence and persisted at least two weeks. Clinically overt jaundice was observed in only 11 patients, two of whom died. Leptospires isolated from the two fatalities subsequently were identified as *L. bataviae* and *L. australis* B. Icterus was also observed in patients infected by organisms in the hebdomadis, canicola, schuffneri, and icterohemorrhagiae serogroups.

Defervescence, usually by crisis, marked the beginning of convalescence. All symptoms and signs promptly subsided, urinary findings returned to normal and icterus, if present, gradually cleared. A few patients experienced a relapse characterized by a return of fever, symptoms, physical signs, and proteinuria for two or three days during the second and third weeks after onset of acute illness. Convalescence was complicated once by thrombophlebitis and another time by unilateral atrophy of the quadriceps muscles. One man suffered two attacks of leptospirosis separated by four months. On these occasions cultures of blood yielded *L. schuffneri* and *L. bataviae*, respectively.

With these exceptions recovery was uncomplicated, and patients resumed their normal activities in three to four weeks.

TABLE 1. Serogrouping of Leptospires of Human Origin in Malaya, 1954-1955

Serogroup	Number of strains
pyrogenes	18
hebdomadis	10
bataviae	10
canicola	9
grippotyphosa	8
autumnalis	8
celledoni	8
icterohemorrhagiae	6
schuffneri	5
australis A	4
javanica	2
pomona	1
djasiman	1
Total	90

Leptospirosis in North America

Sporadic cases and small localized outbreaks of leptospirosis in man occur in the United States. The serogroups represented in this country include icterohemorrhagiae, canicola, pomona[6,7], bataviae,[8] and autumnalis.[9]

Here, as elsewhere, *L. icterohemorrhagiae* produces illness of variable severity. Organisms of the bataviae serogroups exhibit clinical manifestations comparable to classic Weil's disease.[8] *L. canicola* produces slightly different clinical findings.[10] Icterus seldom develops but evidence of an aseptic-type meningitis is common. In all other respects canicola fever resembles Weil's disease.

The leptospire responsible for swineherd's disease was isolated in Pomona, Australia by Derrick[11] in 1942. This agent, *L. pomona,* causes a less serious disease. Fever persists about seven days. Hemorrhagic manifestations are rare and cardiovascular, renal, and hepatic decompensation seldom occur. There is, however, a high incidence of aseptic-type meningitis. In Alabama, Schaeffer[12] has reported the clinical features observed in 26 of 50 patients who were infected by *L. pomona* while swimming in a creek. After an incubation period of two to ten days, those who became ill noted chills and fever, headache, nausea and vomiting, myalgia, and meningismus. Many had conjunctival injection and photophobia. Diarrhea, abdominal pain, and transient maculopapular eruptions were present in a few cases. Lymphocytic pleocytosis and slight elevations of spinal fluid pressures were found in six patients who showed signs of meningitis. After a total illness of five to 14 days, all recovered uneventfully except for a few who experienced a brief uncomplicated relapse.

Beeson,[13] in the United States, and Broom,[14] in England, have identified leptospirosis as a cause of benign serous-type meningitis. Beeson demonstrated significant rises in titers of leptospiral antibodies in 4% of 535 paired sera obtained from patients with meningitis of unknown etiology.

L. autumnalis was first discovered in Japan where it produced a mild febrile illness of seven days' duration in harvesters during the autumn months.[8] Icterus, ocular complications, and death occurred rarely.

In 1943, an illness resembling dengue appeared in soldiers at Fort Bragg, N. C. Daniels and Grennan[15] described the illness. Cardinal features consisted of a short febrile period, moderate prostration, splenomegaly, and a pretibial rash. Extensive investigations were conducted to determine the etiology. Tatlock[16] adapted the agent, thought to be a virus, to several laboratory animals and to fertile hens' eggs. He also reproduced the characteristic signs and symptoms in human volunteers. In 1951, Gochenour,[9] identified the etiologic agent as a leptospire immunogenically similar to organisms of the autumnalis serogroup.

Stroup and Riley[17] recently reported the occurrence of maculopapular lesions over the pretibial area in two siblings presumably infected by *L. pomona.* Both patients became ill eight days after swimming in a stagnant pond where pigs watered. Onset was marked by fever, anorexia and malaise with headache, lethargy and vomiting appearing within 48 hours. Examination on the third day of disease revealed mild muscular tenderness and nuchal rigidity. Proteinuria, microscopic hematuria and mononuclear pleocytosis were also demonstrated. On the fifth day of disease conjunctival injection was noted and maculopapular lesions, resembling erythema nodosum appeared over the pretibial area. After 48 hours, the eruption faded completely. Both patients recovered uneventfully after a total illness of about eight days.

Cultures for leptospires produced no growth. Examination of paired sera from both patients at the Walter Reed Army Institute for Research revealed a marked rise in agglutination-lysis antibody titers against *L. pomona.* Elevations of titers against *L. icterohemorrhagiae* and *L. autumnalis* were demonstrated and interpreted by Gochenour to represent non-specific cross immunological reactions. Serum from another sibling, exposed to the same stagnant pond, revealed antibody titers of 1:100 for *L. pomona, L. icterohemorrhagiae* and *L. sentoti.*

Conclusions

Human leptospiral infections may masquerade as a multiplicity of separate diseases whose clinical features vary considerably. Proper diagnosis may be readily suspected when the classic manifestations of fever, severe prostration, icterus, renal decompensation, hemorrhagic phenomona, and vascular collapse are presented. Milder forms of the disease are most difficult to recognize but a leptospiral etiology should be considered in any febrile patient when severe headache, vomiting, myalgia, conjunctival injection, proteinuria and neutrophilia are noted. Further suspicion is directed toward this diagnosis if there has been exposure to those environmental conditions which favor infection.

REFERENCES

1. Weil, A., Ueber eine eigenthumliche, mit Milztumor, Icterus and Nephritis einhergehende, acute Infectionskrankheit. *Dtsch. Arch. klin. Med.,* 30:209, 1886.

2. Inada, R., Ido, Y., Hoki, R., Kaneko, R. and Ito, H., The Etiology, Mode of Infection and Specific Therapy of Weil's Disease (Spirochaetosis icterohaemorrhagica). *Jour. Exp. Med.*, 23:377, 1916.
3. Noguchi, H., *Spirochaeta icterhaemorrhagicae* in American Wild Rats and its Relation to the Japanese and European Strains. *Jour. Exp. Med.*, 25:755, 1917.
4. McCrumb, F. R., Jr., Stockard, J. L., Robinson, C. R., Turner, L. H., Levis, D. G., Maisey, C. W., Kelleher, M. F., Gleiser, C. A., and Smadel, J. E., Leptospirosis in Malaya I. Sporadic Cases among Military and Civilian Personnel. *Am. Jour. Trop. Med.*, 6:238, (Mar.), 1957.
5. Walch-Sorgdrager, B. Leptospirosis. *Bul. Hlth. Org.*, League of Nations, 8:143, 1939.
6. Gochenour, W. S., Jr., Yager, R. H. and Wetmore, P. W., Antigenic Similarity of Bovine Strains of Leptospirae (United States) and *Leptospira pomona*. *Proc. Soc. Exp. Biol. Med.*, 74:199, 1950.
7. Ashe, W. F., Pratt-Thomas, R. R. and Kumpe, C. W., Weil's Disease; A Complete Review of American Literature and an Abstract of the World Literature, *Medicine*, 20:145, 1941.
8. Gochenour, W. S., Jr., Yager, R. H., Wetmore, P. W., Evans, L. B., Byrne, R. J., Alexander, A., and Hightower, J. A., Indonesian Weil's Disease in Puerto Rico and the United States (abstract). *Fed. Proc.*, 10:408, 1951.
9. Gochenour, W. S., Jr., Smadel, J. E., Jackson, E. B., Evans, L. B., and Yager, R. H., Leptospiral Etiology of Fort Bragg Fever. *Publ. Hlth. Rept.*, 67:811, 1952.
10. Van Thiel, P. H., The Leptospirosis, Leiden, Universitaire Pers Leiden, 1948.
11. Derrick, E. H., *Leptospira pomona*. *Med. Jour. Aust.*, 29, pt. 1:431, 1942.
12. Schaeffer, M., Leptospiral Meningitis; Investigations of a Water-borne Epidemic due to *L. pomona* (abstract). *Proc. Am. Soc. Clin. Invest.*, in *Jour. Clin. Invest.*, 30:670, 1951.
13. Beeson, P. B., and Hankey, D. D., Leptospiral Meningitis. *Arch. Intern. Med.*, 89:575, 1952.
14. Broom, J. C., Leptospirosis in England and Wales. *Brit. Med. Jour.*, 2:689, 1951.
15. Daniels, W. B., and Grennan, H. A., Pretibial Fever, an Obscure Disease. *Jour. Am. Med. Assn.*, 122:361, 1943.
16. Tatlock, H., Studies on a Virus from a Patient with Fort Bragg Fever (pretibial fever). *Jour. Clin. Invest.*, 26:287, 1947.
17. Stroup, J. G., and Riley, H. D., Jr., Pretibial Fever due to *L. pomona*: Report of 2 cases in Siblings. *Jour. Pediat.*, 50:716 (June), 1957.

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Maximum Safe Radiation

Sharp revision in present estimates of "safe" doses of radiation may be necessary if experiments of some investigators are confirmed.

Dr. Michael A. Bender of Johns Hopkins University warned that the National Academy of Science maximum permissible dose (m.p.d.) of 10 r. may be much too high, according to report in *Medical News*. Doctor Bender described his experiments of subjecting normal tissue to known doses of radiation, then carefully measuring resulting genetic damage as chromosome breakage.

Treatment of Leptospirosis in Animals

(Continued from page 547)

antibiotics in the feed is particularly noteworthy for the treatment of leptospiruria in large animals because of the economy, the simplicity, and the limited labor involved.

Summary

In summary, the treatment of leptospirosis involves the use of agents to destroy organisms whether present in circulatory fluids or localized in the kidney and the use of extensive supportive therapy to overcome effects produced by infection, particularly effects upon the kidney, liver, and erythrocytes. And further, that the supportive therapy employed should be governed by the knowledge of what has occurred and what is likely to occur as a result of infection.

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Research Bulletins on Chinchilla

Six new research bulletins on chinchilla which will be of interest to veterinarians have been published by National Chinchilla Breeders of America, Inc. There is no charge for these bulletins to veterinarians, laboratories, research groups and educational institutions.

The new, bulletins are: #29 — Egg Loss in the Chinchilla, by Howard H. Hillemann, M.A., Ph.D. and F. Donald Tibbitts, M.A. of Oregon State College; #30 — Antibiotic Feeding, by R. Keith Farrell, D.V.M.; #31 — Ovarian Growth and Development in Chinchilla, by Dr. Hillemann and Mr. Tibbitts; #32 — Cecal Impactions, by Dr. Farrell; #33 — Reproductive Potential in Chinchilla, by Dr. Hillemann and Mr. Tibbitts; #34 — Reproductive Performance in Chinchilla, by Dr. Hillemann and Mr. Tibbitts.

NCBA has 29 research bulletins available at this time, including the six already mentioned, and all may be ordered from NCBA, P. O. Box 145, Middletown, N. Y. Veterinarians who wish to receive these bulletins automatically without charge as they are published should request NCBA to place their name on the permanent mailing list to receive NCBA Research Bulletins.

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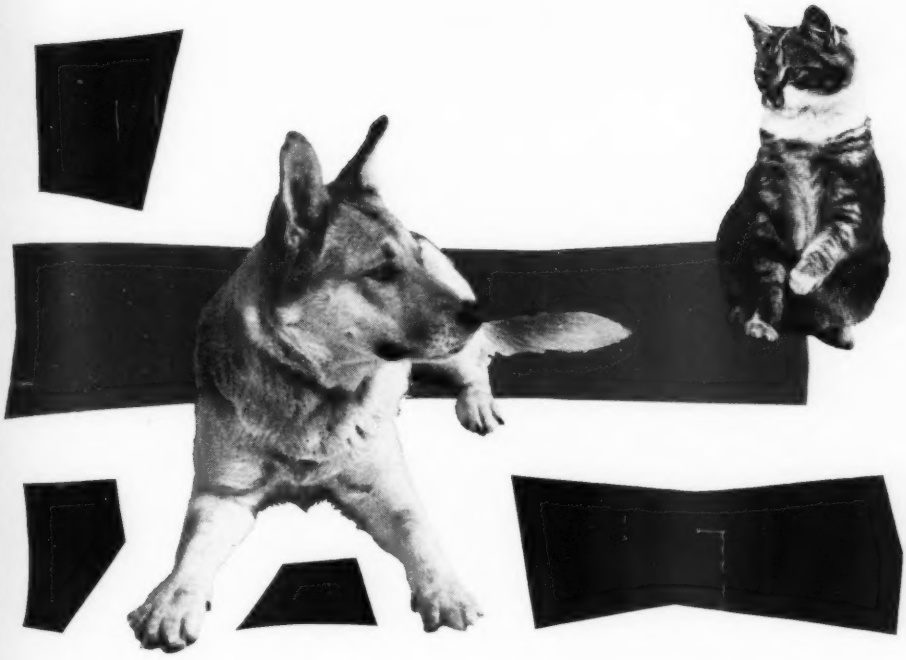

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The Sylvatic And Ecological Aspects Of Leptospirosis†

HERBERT G. STOENNER,* D.V.M., Hamilton, Montana

MANY aspects of sylvatic leptospirosis have been discussed in previous papers. I will try to limit my remarks to some that were not described in detail.

Species Susceptibility

With few exceptions, the primary hosts of most pathogenic serotypes of Leptospira are rodents. For example, *Leptospira icterohemorrhagiae, L. australis, L. pyrogenes,* and *L. bataviae* are found principally in the members of genus Rattus. *L. ballum* and *L. grippotyphosa* are found predominantly in mice, and *L. hebdomadis* principally in voles. As an exception, the dog is the primary host of *L. canicola.* Cattle and swine are possibly primary hosts of *L. pomona.* However, in Denmark, a rodent, *Apodenemus agrarius,* has been found to be a reservoir of *L. pomona,*[1] and as Doctor Steele indicated this morning other reservoirs may be found. Sometimes it is difficult to distinguish between the primary reservoir of a particular serotype and a secondary host. Though cattle and swine may not be primary hosts, epizootics which do not originate from other host species occur among these domestic animals.

Generally, in nature, each serotype is found principally in a single species of rodent but under certain conditions one serotype may occur in several host species. This depends upon the number of species of rodents in a particular habitat and the extent of interspecies contact between rodents in such an environment. Usually, only a single serotype may be isolated from an individual rodent, but occasionally a single animal may harbor more than one serotype. One feature that is characteristic of a primary host is an almost perfect balance between the Leptospira and the host. Another characteristic is that leptospires are constantly leaving the body of the host; because the organism is readily destroyed by unfavorable environmental factors, large numbers must be eliminated to insure contact with a new host. Once a rodent is infected, it generally remains infected for life and continuously eliminates varying numbers of leptospires in its urine.

Pathogenesis

The pathogenesis of leptospirosis in rodents is essentially the same as that in domestic animals. Skin abrasions and mucous membranes may serve as atria for the entrance of leptospires. Subsequently, a period of leptospiremia occurs and the organism can be demonstrated in the blood stream; after development of humoral immunity, leptospires localize in the tubules of the kidney where they are separated from humoral antibody. Actually, urine of infected animals does contain antibodies, but whether such antibody is present at the site of multiplication of the organism is questionable. Pathologic changes in the kidneys of some animals are sufficient to permit antibodies from the blood stream to escape into the urinary side of the tubules. In rodents, the population of leptospires in the kidney is sometimes phenomenal. One may be amazed at the number that grow from a bit of infected kidney incubated in Verwoort's medium for 48 to 72 hours. Usually population of leptospires in rodent renal tissue is much heavier than that seen in domestic animals such as dogs, cattle, or swine. That leptospirosis of rodents is entirely an inapparent infection is generally assumed. However, the extensive kidney damage observed in some rodents must affect their health. In fact, during an outbreak of *L. grippotyphosa* infection among rodents, Gsell[2] related that weak or moribund animals were caught easily.

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†Presented at the Interprofessional Symposium on Leptospirosis, Postgraduate Medical Study, University of Kansas Medical Center, Kansas City, Kansas, April 25, 1957.

*From the U. S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, National Institute of Allergy and Infectious Diseases, Rocky Mountain Laboratory, Hamilton, Montana.

TABLE 1. Prevalence of Leptospirosis (*L. ballum*) in Immature Swiss Albino Mice Determined by Serologic Findings and Culture of Kidneys

Age	Serology		Culture	
	Pos.*	Neg.	Pos.	Neg.
1 day before nursing**	4	1	Not tested	
2 days*	5	0	Not tested	
7 days**	10	2	0	12
21 days	18	14	0	32
35 days***	2	8	0	10
51 days***	2	8	0	10
65 days***	0	10	0	10

*Complete reaction in 1:10 dilution by agglutination-lysis test. **Pool of 3 or 4 litter mates. ***Progeny of seropositive female mice.

Incidence of Infection

The incidence in a particular population of rodents depends upon the density of rodent population and the environmental factors that affect survival of leptospires. For example, a high incidence is found among rodents in rice fields where there is ample food supply and ample moisture to enhance the survival of these leptospires. Most studies of rodents have involved investigations of the incidence of *L. icterohemorrhagiae* among various species of the genus Rattus. Middleton[3] found 41.7% of rats in Oxford infected with *L. icterohemorrhagiae* and the highest incidence of infection among the oldest age groups. Mason[4] in Liverpool found that a third of the rats he examined were infected. Lewis[5] determined that 11% of rats in Philadelphia were infected, and Pawan[6] found that 26.6% of the rats in Trinidad were carriers. In most studies in which infection rates have been correlated with age, immature rodents are essentially free of leptospires, and the highest incidence has been found among the older age groups. The reason for this distribution may be explained by the following results of studies made on a colony of Swiss albino mice infected with *L. ballum*.

Incidence in Mouse Colony

Infection of mice at the Rocky Mountain Laboratory was first recognized in 1949, and the organism has remained in our colony since that time. Recently, we recognized that this disease in mice constituted a health hazard for our employees and we are now conducting studies to eliminate leptospirosis from our colony.

In order to determine the prevalence of leptospirosis in the colony, mice were bled and then their kidneys were cultured in Verwoort's medium. If a culture of kidney contained bacterial contaminants, the serum from this animal also was excluded from the data. The highest infection rate was found among older mice, such as discarded breeding females (tables 1 and 2). Leptospires were readily isolated from mature mice that were serologically positive. Since most dams in the colony were shedding organisms in their urine, a high infection rate among immature mice was expected. True, a high percentage of baby mice possessed antibodies, but leptospires could not be isolated from their kidneys. Further studies revealed a direct relationship between antibody levels of baby mice and antibody titers possessed by their dams (table 3). These data suggested that antibodies possessed by immature mice were passively acquired from their mothers. The presence of antibody in serums of mice at birth was a surprising observation. However, the very intimate placentation of rodents apparently permits maternal antibodies to diffuse into the fetal circulation. After ingestion of colostrum, antibody titers of baby mice increased and reached levels about five to tenfold lower than those of their respective dams. In some mice, these antibodies could still be detected by serologic tests at 51 days of age but not at 65 days. The last three groups of mice (table 1) were weaned at 21 days of age from serologically positive dams; although serologically negative mice of this age are susceptible, none contracted the disease from their mothers. Results of the preceding studies indicate that passively acquired antibodies protect immature mice. These observations may explain the low incidence of infection among immature rodents under conditions in nature.

Environmental Factors

The moisture content of an environment is of primary importance in the ecology of

TABLE 2. Prevalence of Leptospirosis (*L. ballum*) in Mature Swiss Albino Mice Determined by Serologic Findings and Culture of Kidneys

Classification	Serology		Culture	
	Pos.*	Neg.	Pos.	Neg.
Male (114-day-old breeding stock)	13	2	14	1
Female (114-day-old breeding stock)	13	4	13	4
Female (random sample)	33	5	33	5
Female (discarded breeding stock)	63	6	63	6

*Complete reaction in 1:10 dilution by agglutination-lysis test.

leptospires because these organisms do not survive long without moisture. The pH of the environment is also of importance. In East Sumatra, Sardjito and Zuelzer[7] found leptospires in waters of pH 7.4 to 7.6. In this area the soil had a high sodium and magnesium content. In West Java, where soil of volcanic origin had a low sodium and magnesium content and waters had a pH of 5.7 to 6.7, leptospires could not be demonstrated. Taylor and Goyle[8] found leptospires in the Adamans in waters of pH above 6.9.

In the state of Washington, the highest incidence of bovine leptospirosis was recognized east of the Cascade range where soil and water were alkaline, between pH 7.0 and 8.0. Gillespie and associates[9] were able to recover *L. pomona* from streams and surface pools which had been contaminated with urine of recovered cattle. In one instance, they recovered *L. pomona* from surface waters ten days after cattle had been removed from the pasture. In another instance, *L. pomona* was recovered from a stream flowing 252,100 gallons per minute; the sample examined was taken downstream from the watering site of infected yearling calves.

Heretofore, leptospirosis has been considered to be a tropical disease because freezing temperatures were presumed to exert a deleterious effect on the organism. In contrast, most outbreaks observed in Washington occurred during mid-winter; this indicates that the survival of the organism at freezing or near-freezing temperatures is adequate to perpetuate an epizootic.

Bacteria which compete for nutrients in an environment, particularly those that affect acid changes in pH, are detrimental to the survival of leptospires. Hence, cultures of Leptospira may be destroyed by contaminants whose end products of metabolism acidify the medium. Leptospires in milk are soon destroyed by contaminating bacteria.

Summary

The primary hosts of most pathogenic serotypes of leptospires belong to the rodent family. Usually, each serotype is peculiar to certain species of rodents. Once infected, the host-parasite balance results in a permanent population of leptospires in the kidneys of rodent carriers. The highest incidence of infection is found among older rodents, and immature animals presumably are protected by humoral immunity passively acquired from their mothers.

TABLE 3. Relationship between Antibody Titers of Dams and Antibody Titers of Suckling Mice*

Litter No.	Dams	Progeny** Before nursing	2 day old	7 days old
1	500	10	100	
2	5,000	10	500	
3	5,000	10	100	
4	5,000	100	500	
5	100	0	100	
6	100			10-100
7	500			100-100
8	5,000			100-500
9	5,000			100-500
10	5,000			500-500
11	0			0-0

*Numbers are reciprocals of titers. **All pools of 3 or 4 immature mice.

Ecological conditions that are prerequisite to an epizootic of leptospirosis may be described as follows: First, the source must be a carrier that is shedding leptospires in its urine. Second, leptospires must be deposited in a moist environment with proper pH and other attributes that enhance their survival. Third, a susceptible animal, whether man, domestic animal, or rodent, must contact the freed organisms in their environment. Under these conditions, cycles of infection continue until one or more prerequisites are removed.

REFERENCES

1. Borg Petersen, C., Fennestad, K. L., A Field Rodent (*Apodenemus agrarius*) as Carrier of *Leptospira pomona* in Denmark. *Jour. Am. Vet. Med. Assn.*, 128:204, 1956.

2. Gsell, O. R., Symposium on the Leptospiroses. Washington, D. C. Army Medical Service Graduate School, Walter Reed Army Med. Center, 1952.

3. Middleton, A. D., *Leptospira icterohaemorrhagiae* in Oxford Rats. *Jour. Hyg.*, 29:219, 1929.

4. Mason, W. N. M., The Incidence of Leptospiral Infection in Rats in Liverpool. *Jour. Path. and Bact.*, 46:631, 1938.

5. Lewis, M., The Incidence of *Leptospira icterohaemorrhagiae* in Trapped Rats in Philadelphia. *Am. Jour. Trop. Med.*, 22:571, 1942.

6. Pawan, J. L., *Leptospira icterohaemorrhagiae* in Rats in Trinidad, B.W.I. *Ann. Trop. Med. and Parasitol.*, 25:31, 1931.

7. Sordjito, M. and Zuelzer, M., Weiterer Beitrag zur Biologie der *Spirochaeta biflexa* syn. *Leptospira icterohaemorrhagiae*, syn. *Spirochaeta icterogenes* in den Tropen. *Centralbl. Bakt. I.* Abt. Orig. 110:180, 1929. *Biol, Abst.*, 4:1822, 1930.

8. Taylor, J. and Goyle, A. N., Leptospirosis in the Adamans (with an Appendix on the Present Knowledge of Leptospiral Infections). *Ind. Med. Res. Mem.*, 20:1, 1931. *Biol. Abst.*, 6:1132, 1932.

9. Gillespie, R. W. H., Kenzy, S. G., Ringen, L. M., and Bracken, F. K., Studies on Bovine Leptospirosis. III. Isolation of *Leptospira pomona* from Surface Waters. *Am. Jour. Vet. Res.*, 18:76, 1957.

Significance Of The Leptospiroses In Military Medicine†

LT. COLONEL LESLIE C. MURPHY,* V.C., U. S. ARMY, and AARON D. ALEXANDER,* M.S., Washington, D. C.

RECENT reports of outbreaks of leptospiroses among British troops in Malaya[1-3] and among French troops in Indo-China[4] have again focused attention on these diseases as potential military hazards. The military significance of leptospirosis was first recognized in World War I when epidemic outbreaks of spirochetal jaundice or Weil's disease occurred among British, German, French, and Belgian troops who were engaged in trench warfare along the Western front.[5-8] At the same time, this disease was also reported among Italian troops in northern Italy and among Canadians in Salonika.[9] The leptospiral etiology of this disease was demonstrated by independently conducted investigations on the Western Front by research workers in the Army Medical Services of Germany, France, and Britain.[10-13] This confirmed the observation of Inada *et al.*[14] in Japan in 1915 and provided additional clinical and laboratory information on Weil's disease. These European and Japanese investigators called attention to the then rarely recognized syndrome which was first described by Weil in 1886,[15] and they provided the stimulus for worldwide studies.

Following World War I, Weil's disease was recognized throughout the world and the high infectivity rates of Norway rats, the primary hosts, were reported in many countries.[9] The protean manifestations of Weil's disease were recognized and the classically described hepatonephritic syndrome was found to occur less frequently than had previously been recognized.[9,16,17] In addition, other diseases attributable to leptospires that differed serologically from the classical strain (*L. icterohemorrhagiae*) were found in domestic animals as well as in man, and the distribution of numerous serologically distinct strains, potentially infective for man among numerous rodent or other mammalian species, was also demonstrated. These investigations led to the concept that the leptospiroses were a group of diseases caused by distinct members of the spirochetal genus Leptospira.[18]

Leptospirosis in Troops after World War I

During the period between World Wars I and II sporadic cases and outbreaks of leptospirosis were reported among military personnel in various parts of the world. In Great Britain, Weil's disease was found in four soldiers who had bathed in a local canal in a rat infested area,[19] and a case was reported in a stableman who provided a history of association with a rodent and a dog.[19] Infectious jaundice, presumably caused by leptospirosis was also noted among troops in India[20] and Indo-China.[4] More important were reports in troops, for the first time, of outbreaks of leptospirosis, more frequently anicteric, attributable to serotypes other than *L. icterohemorrhagiae*. In Russia, cases of leptospirosis due to *L. grippotyphosa*, the etiologic agent of swamp fever, occurred among soldiers who had bathed in a river located near their encampment.[21] At the same time, an epidemic of *L. grippotyphosa*, as well as *L. andaman* leptospirosis, broke out among inmates and military personnel of a prison camp in the Andaman Islands.[20] Seventy-three cases, with a case fatality rate of 18.7%, were observed in this outbreak, which was associated with working in water-logged land.

At the outbreak of World War II, a considerable mass of data dealing with the various epidemiological, clinical, and laboratory aspects of leptospirosis was available. However, most of this information did not gain universal recognition. The concept of leptospirosis, in this as well as other countries, was for the

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*Department of Veterinary Bacteriology, Division of Veterinary Medicine, Walter Reed Army Institute of Research.

most part synonymous with Weil's disease, and only the relatively infrequent icteric aspects of this disease were recognized, a concept which unfortunately still prevails to a considerable extent. In addition, during the World War II, trench warfare was obsolete and presumably the absence of this type of warfare, which posed a serious problem of infection with spirochetal jaundice in World War I, served to divert attention from the infection hazard of leptospirosis in these military campaigns. However, severe epidemic outbreaks of leptospirosis were reported during this period. Bulmer[23] estimates that at least 100 cases of Weil's disease occurred at the Normandy beachhead among British soldiers who used local streams for washing and bathing. Subsequently, evidence of the occurrence of "mud fever" (*L. grippotyphosa* and *L. sejroe* infections) in addition to Weil's disease was uncovered in 1945 in British patients who were exposed to the wet soil of France.[23] In 1940, an epidemic of *L. grippotyphosa* leptospirosis broke out among German soldiers in the Valley of Charente.[24] The disease was anicteric and cases only occurred in soldiers who had bathed in the river. It is noted that the leptospiral etiology was not considered until local inquiry revealed that this region was an area of endemic leptospirosis. Explosive outbreaks of Weil's disease were also reported among troops in Bulgaria[25] and in Italy.[26] In both countries, the outbreaks were associated again with a history of bathing in local waters.

It is difficult to assess the true incidence of leptospirosis in World War II. In retrospect it is now recognized that combat was conducted in many hyperendemic areas of leptospirosis and under conditions which would favor the spread of these diseases. Tabulations of the medical records of the U. S. Army for 1944-1945 indicate that 25 cases of Weil's disease and three deaths were reported among U. S. Army personnel in the Pacific areas. Five cases and no deaths from Weil's disease were reported for the China-Burma-India Theater for the same period. It is probable that these few cases represent only a fraction of the total number of actual cases in troops who were engaged in combat under primitive sanitary conditions in wet jungles. New Guinea, for example, is an area where 55% of the indigenous population showed evidence of past or recent infection with leptospirosis.[27]

The absence of adequate diagnostic facilities and the general unawareness of the manifold clinical and epidemiological aspects of these diseases may have been significant contributory factors in our failure to detect leptospirosis in World War II. That epidemics of these diseases may occur without recognition of the etiology is strikingly illustrated by the outbreaks of a febrile, anicteric disease during the summers of 1942, 1943, and 1944 at the military reservation at Fort Bragg, North Carolina.[28,29] Approximately 40 cases occurred in each of the three years it was observed. The disease was a nonfatal febrile illness of about five days' duration, associated with headache, malaise, and splenomegaly. The most distinctive feature of the disease was the appearance of an erythematous rash on about the fourth day of illness and was usually limited to the pretibial areas of both legs. An infectious agent which induced a fatal disease in hamsters, a mild febrile illness in guinea pigs and rabbits, and grew in embryonating eggs was isolated. Volunteers inoculated with the agent developed an illness indistinguishable from Fort Bragg fever. This disease was considered of viral origin until Gochenour, nine years later, tested convalescent sera and found a high level of agglutinating antibody against *L. autumnalis*. With this lead a leptospiral organism was recovered from material of the 259th hamster passage of the Fort Bragg agent.

Similarly, an outbreak of "aseptic" meningitis among American troops in Okinawa in 1949 was attributed to leptospirosis three years later.[30] Of 19 patients with symptoms of a central nervous disease, 16 were shown by serologic methods to have leptospiral infection as demonstrated by a rise in aggluntinin titers to a member of the *L. hebdomadis* group. This outbreak serves to emphasize how easily leptospiral infections of the central nervous system can be overlooked. In this group of patients, the common exposure to surface waters led to a brief consideration of leptospirosis and the disease was clinically diagnosed as encephalitis of unknown cause. Leptospirosis was not considered again as a possibility until long after these cases had occurred and laboratory tests had eliminated a number of known viral agents as being of etiological significance.

During the Korean conflict, leptospiral diagnostic laboratory facilities were available and medical personnel were alerted to the potential infection hazard of these diseases. However, although these infections were enzootic in Korean wild life, leptospirosis in this conflict was not a military medical problem. In large measure, this was attributed to the nature of

the terrain in which troop movement and fighting occurred, to the intensive rodent control exercised because of their importance in epidemic hemorraghic fever, and to the high sanitary discipline of the troops, particularly with respect to water sanitation.[21]

In recent years, in addition to the Okinawa epidemic, outbreaks of *L. grippotyphosa* and *L. pomona* leptospirosis have been reported among troops in France[23] and Yugoslavia[28] respectively. Both epidemics were associated with bathing episodes. The potential infection hazard of leptospirosis in troops has been signally realized in the recent military operations in Malaya and Indo-China. Since 1951 more than 100 cases of leptospiral infection caused by multiple serotypes were found annually in British troops engaged in jungle warfare against communist bandits in Malaya.[1,2,3,4] Thirty-five per cent of all illness in the military in this area was attributed to leptospirosis[2]; an incidence rate that was remarkably higher than all other known pyrexias combined, including malaria, scrub typhus, and dengue. Attack rates of 63 and 30 (cases per 1,000 troops at risk per annum) were observed in the operational area of Pahang during 1954 and 1955, respectively. Similarly, in Indo-China extensive epidemics of leptospirosis occurred in 1950 to 1952 among North African and European troops who traversed or operated in water and mud.[4] In a single operation, for example, 126 soldiers (25% of the effective force) were infected with these spirochetal diseases.

The leptospiroses in troops as well as in civilians are accidental infections with organisms which are normally found in numerous species of rodent and other mammalian species as well as in domestic animals. However, military operations, in combat or peacetime maneuvers, are usually carried out under improvised sanitary facilities and under climatic and terrain conditions that may introduce all of the factors conducive to the spread of leptospirosis in man.

Seasonal factors are obviously important in governing terrain conditions and in affecting the occupational or recreational activities of man. In this respect it is worthwhile to note again that many of the epidemic outbreaks of leptospirosis in troops have been associated with bathing episodes.[21,22,24-29,30,32,33]

Problems of Leptospirosis in Military Medicine

Obviously, the extensive presence of leptospirosis in omnipresent natural hosts, the survival of these organisms in aquatic environments, and their ability to readily invade a highly susceptible human host, should direct attention to the leptospiral infection hazard in troops who traverse or otherwise come into contact with streams, marshes, swamps, flooded or muddy areas that may be contaminated with animal urine. Certainly the recent experience in Malaya and Indo-China indicate that leptospirosis may be a major cause of disease in troops operating under the above conditions. In addition, the wartime devastation of developed areas and the disruption of modern sanitary facilities may preface the rodent infestation of a terrain ideally modified for the epidemic spread of these diseases in civilian as well as military populations.

From the military point of view, the reduction in the operational force by the hospitalization of patients, which frequently may be protracted, is of course a significant aspect of leptospirosis in troops. In addition, other aspects of leptospirosis pose problems in military medicine — problems of clinical and laboratory diagnosis, therapy, prophylaxis, and control, as well as problems related to the health of dogs closely associated with troops and the health of larger domestic animals which provide an important source of food.

TABLE 1. 480 Cases of Aseptic Meningitis, Percentage of Cases Diagnosed in the Laboratory, Army Medical Service Graduate School, 1947-1952

Diagnosis	Number Cases Tested	Proved Cases No.	Proved Cases %	Probable Cases No.	Probable Cases %	No.	Total Cases Percentage Minimal[1]	Total Cases Percentage Maximal[2]
LCM	454	37	8.1	7	1.6	44	9.2	9.7
Mumps	445	42	9.4	17	3.9	59	12.3	13.3
Herpes	114	6	5.3	—	—	6	1.2	5.3
Leptospirosis	158	12	7.6	—	—	12	2.5	7.6
Total	480						25.2	35.9

[1]Percentage of 480 cases actually diagnosed. [2]Percentage of 480 cases which would have been diagnosed if the proportions in those tested had applied to the entire group.

TABLE 2. Etiologic Study of 416 Cases of "Viral" CNS Disease (WRAIR 1953-1956)

Etiology of Case	Number of Diagnosed Cases by Clinical Syndrome: Aseptic Meningitis	Paralysis	Encephalitis
Poliomyelitis	20	79	1
Mumps	41	6	8
Lymphocytic Choriomeningitis	28	2	4
Herpes Simplex	6	3	5
Arthropod Encephalitis	2	2	10
Leptospirosis	12	0	0
Tuberculosis	4	0	1
Coccidiomycosis	1	0	0
Coxsackie	4	0	0
Orphan	13	0	0
Total Diagnosed	131	92	29
Total Undiagnosed	106	26	32
% Diagnosed	55%	78%	32%

Diagnosis

Fundamentally, the most important problem in military medicine with respect to human leptospirosis is that of recognition. The developing symptoms may vary considerably from severe icteric-hemorrhagic manifestations accompanied by renal insufficiency to benign catarrh-like presentations.

Because of this diverse symptomatology, it is necessary to differentiate the leptospiroses from a host of other diseases. It is significant that many outbreaks characterized by rash, meningitis, or other nonicteric symptoms are frequently recognized in retrospect as was the case in the Okinawa and Fort Bragg epidemics.[29,35] More recently, studies on the etiology of the so-called "abacterial" meningitides, conducted at the Walter Reed Army Institute of Research, as well as at other institutions, have shown that leptospirosis accounts for 3 to 10% of these undiagnosed fevers.[36-38]

Table 1 summarizes 480 cases of aseptic meningitis studied between 1947-1952.[38] Serologic tests for a wide spectrum of serotypes of leptospires were performed. Diagnosis of infection with one of these serotypes was regarded as established if a fourfold increase in antibody titer was demonstrable during convalescence. A presumptive diagnosis was made if antibodies were present in a titer of 1:400 or greater in the early convalescent stage of central nervous system illness. Nine cases of leptospiral meningitis were found in a random sample of 91 patients with aseptic meningitis who failed to yield serologic evidence of infection with lymphocytic choriomeningitis (LCM) or mumps viruses. The remaining three cases were detected among 67 cases of aseptic meningitis studied between June 1951 and June 1952. During this time serologic tests for leptospiral infections were included as part of the diagnostic studies on all cases of aseptic meningitis. In four of these 12 patients, possible exposure to leptospirosis in lower animals was recorded. One patient had assisted in the vaccination of cattle, a second had drunk river water, a third had been working on a farm with sick swine, and a fourth was a practicing veterinarian in a small animal clinic.

Table 2 summarizes results obtained at Walter Reed during the past three years in a study of such cases.[39] Twelve cases clinically diagnosed as aseptic meningitis of a total of 131 were proved to be leptospirosis by serologic methods in which a rise in titer in acute and convalescent sera was shown.

Of paramount importance in the diagnosis of leptospirosis is the history elicited from the patient. Undiagnosed fevers associated with a history of direct contact with wild or domestic animals or contact with streams, ponds, damp trenches and foxholes, marshes, swamps, rice paddies, etc., should provide a high index or suspicion of leptospirosis.

Laboratory confirmation of the diagnosis of leptospirosis can be easily established bacteriologically or serologically if proper laboratory procedures are initiated during the course of disease.

The technics for the laboratory diagnosis of leptospirosis are the subject of another paper this afternoon; however, I would like to mention a problem in diagnosis that the military has that may not be as acute in civilian laboratories. This is the shipment of serum specimens which must be refrigerated since preservatives would affect the live antigens employed in diagnostic tests such as the leptospiral agglutination tests. We have recently studied serum specimens from four species of animals and man by comparing the agglutinin titers between equal amounts of sera preserved by freezing and by drying on an adsorbent paper. Results of this study indicate that agglutinins are unaffected by adsorption and drying on paper and this method is a convenient one for shipping sera long distances.

The effective control of human leptospirosis by vaccine prophylaxis was demonstrated early in the history of leptospirosis by Wani.[40] Im-

munization against leptospirosis in man has not received broad application. In human leptospirosis the prophylactic efficacy of vaccination with formalin-treated suspensions of leptospires was demonstrated in extensive field trials conducted among rice-field workers in Italy and Spain. The vaccines were polyvalent, prepared from two serotypes and elicited no untoward response.

From the military viewpoint, the incidence of leptospirosis in troops has not been sufficiently high to warrant the routine immunization of troops. It has not been feasible at this time to prepare a polyvalent vaccine which would afford protection against the numerous serotype strains. The selection of serotypes for the preparation of vaccines would vary in different parts of the world. In some areas of multiple leptospirosis such as Malaya, it may be possible to prepare a polyvalent vaccine which would protect against infections by the more frequently occurring serotypes; however, further studies on the efficacy of polyvalent vaccines in cross-protection against a multiplicity of serotypes is desirable.

Control

Perhaps the most important aspect of control of leptospirosis is the education of troops to infection hazards and to sources and modes of infection. The current methods in military sanitation embody many principles which can arrest the spread of leptospiral diseases. The significance of strict observance of sanitary discipline, particularly with respect to the chlorination of water used for drinking, bathing, and washing; rodent control, protection of food and water from contamination, prohibition of swimming or bathing in ponds, streams, or other waters, should be emphasized.

The health of domestic animals has an important bearing on military medicine. Dogs are intimately associated with troops either as service animals or mascots. Leptospirosis in the larger domestic animals is significant since they may serve as potential sources of infection. In addition, these diseases are important in so far as they affect the health and productivity of animals, which are important to food supply, particularly in times of war.

Summary

The high attack rates of leptospirosis among the British troops in Malaya and the French troops in Indo-China have again focused attention on these diseases as potential military hazards. In the military history of leptospirosis since World War I, the sporadic epidemic outbreaks caused by *Leptospira icterohemorrhagiae* and other leptospiral serotypes during the periods of peace and war, have been reviewed. It is notable that the leptospiral etiology was not recognized in several epidemic outbreaks at the time of occurrence. Leptospires were probably important etiologic agents in undiagnosed febrile diseases that occurred during World War II in troops operating in hyperendemic areas of leptospirosis. The failure to recognize leptospirosis was due in part to the general unawareness of the more frequently occurring, nonicteric, protean manifestations of these diseases. Other factors that contribute to missed diagnoses of leptospirosis are related to the peculiar bacteriological and serologic properties of leptospires that preclude their detection by routine laboratory diagnostic procedures. The important epidemiological factors that operate in the transmission of these diseases have an important bearing on the potential infection hazards of troops operating under improvised sanitary conditions in peacetime or wartime maneuvers. Leptospiral diseases pose problems in military medicine related to clinical and laboratory diagnosis, treatment, prophylaxis and control. In addition, the occurrence of leptospirosis in domestic animals is important in military medicine since these animals may serve as potential sources of infection. These diseases may affect the health and productivity of animals which are important to the food supply, particularly in times of war.

REFERENCES

1. Broom, J. C., Leptospirosis in Tropical Countries. A review. *Trans. Roy. Soc. Trop. Med. Hyg.*, 47:273, 1953.

2. McCrumb, F. R., Jr., Stockard, J. L., Robinson, C. R., Turner, L. H., Levis, D. L., Kelleher, H. F., Gleiser, C. A., and Smadel, J. E., Leptospirosis in Malaya, I. Sporadic Cases Among Military and Civilian Personnel. *Am. Jour. Trop. Med. Hyg.*, to be published.

3. Robinson, C. R., and Kennedy, H. F., An Investigation into the Clinical and Laboratory Features of an Outbreak of 31 Cases of Anicteric Leptospirosis. *Jour. Roy. Army Med. Corps*, 102:196, 1956.

4. de Lajudie, P., and Brygoo, E. R., Less Leptospiroses au Viet-Nam. *Med. Trop. Marseille*, 13:466, 1953.

5. Stokes, A., Ryle, J. A., A Note on Weil's Disease (*Spirochaetosis icterohemorrhagica*) as it Occurred in the Army in Flanders. *Brit. Med. Jour.*, 2:413, 1916.

6. Uhlenhuth, P., Epidemiologie der Weil'schen Krankheit. *Acta Conv. Tert. de Trop. Morbis*, 1:357, 1938.

7. Garnier, M. M., and Reilly, M. J., L'ictere Infectieux a Spirochetes. *Bul. Mem. Soc. Med. Hop. Paris*, 40:2249, 1916.

8. Renaux, E., Note sur la *Spirochetose icterohemorhagique*. *Compt. Rend. Soc. Biol.*, 79:947, 1916.

9. Walch-Sorgdrager, B., Leptospirosis. League of Nations Bul. Health Organization, 8:143, 1939.

10. Uhlenhuth, P., and Fromme, W., Experimentelle Untersuchunger uber die sogenannte Weilsche Krankheit (Ansteckende Gelbsucht). *Med. Klin.*, 11:1202, 1915.

11. Huebner, E. A., and Reiter, H., Beitrage zur Aetiologie der Weilschen Krankheit. *Deut. med. Wochschr.*, 41:1275, 1915.

12. Martin, L., and Pettit, A., La *Spirochetose icterohemorrhagique* en France. *Presse med.*, 24:569, 1916.

13. Dawson, B., and Hume, W. E., Jaundice of Infective Origin. *Quart. Jour. Med.*, 10:90, 1916.

14. Inado, R., Ido, Y., Koki, R., Kaneko, R., and Ito, H., The Etiology, Mode of Infection, and Specific Therapy of Weil's Disease. *Jour. Exp. Med.*, 23:377, 1916.

15. Weil, A., Uber eine eigenthumliche, mit Milztumor, Icterus und Nephritis einhergehende acute Infectionskrankheit. *Deut. Arch. klin. Med.*, 39:209, 1886.

16. Gsell, O., Leptospirosen. Verlag Hans Huber, Bern, 1952.

17. van Thiel, P. H., The Leptospirosis. Universitaire pers Leiden, Leiden, 1948.

18. Coles, W. E. K., Leptospirosis in Aldershot Command. *Jour. Roy. Army Med. Corps*, 66:73, 1936.

19. Wigmore, J. B. A., and Denning G. M., Leptospiral Jaundice in a Groom. *Jour. Roy. Army Med. Corps*, 66:21, 1936.

20. Taylor, J., and Goyle, A. N., Leptospirosis in the Andamans. *Indian Med. Res. Memoir*, 20:1, 1931.

21. Simonenko and Brill (1928) Quoted by van Thiel (Ref. 7).

22. Bulmer, E., Weil's Disease in Normandy: Its Treatment with Penicillin. *Brit. Med. Jour.*, 1:113, 1945.

23. Buckland, F. E., and Stuart, R. D., Mud Fever in the British Army in France. *Lancet*, 2:331, 1945.

24. van Hoesslin, H. Zur Kenntnis des Feld-(Schlamm-) Fiebers. *Med. Clin.* (Munich), 37:753, 1941.

25. Ostertag, H., Leptospirosis icterohemorrhagiae in Bulgarien. *Z. Hyg. Infektionskrankh.*, 131:482, 1950.

26. Hutchison, J. H., Pippard, J. S., and Gleeson-White, M. H., Outbreak of Weil's Disease in the British Army in Italy. I. Clinical Study. *Brit. Med. Jour.*, 1:81, 1946.

27. Forbes, B. R. V., Leptospiral Infection in Natives of the Territory of Papua and New Guinea. *Australasian Ann. Med.*, 4:64, 1955.

28. Daniels, W. B., and Grennan, H. A., Pretibial Fever. *Jour. Am. Med. Assn.*, 122:361, 1943.

29. Tatlock, H., Studies on a Virus from a Patient with Fort Bragg Fever (Pretibial Fever). *Jour. Clin. Invest.*, 26:287, 1947.

30. Gauld, R. L., Crouch, W. L., Kaminsky, A. L., Hullinghorst, R. L., Gochenour, W. S., Jr., and Yager, R. H., Leptospiral Meningitis. Report of Outbreak among American Troops on Okinawa. *Jour. Am. Med. Assn.*, 149:228, 1952.

31. Yager, R. H., Leptospiroses. Recent Advances in Medicine and Surgery. *Med. Sci.* Publ. No. 4, vol. 2:330, 1954.

32. Lefebvre des Noettes, R. A., Seigneuric, C., and Kolochine-Erber, B., Contribution a l'Etude de la Leptospirose a *"Leptospira grippo-typhosa"* Fievre des Marais, Fievre de la Vase: Une Epidemie Estivale de 77 Cas en Milieu Militaire. *Presse med.*, 58:1189, 1950

33. Bordjoski, M., Vojnosanitotski Pregleg, 9:90, 1952. (Quoted by Gsell, O., ref. 39.)

34. Fairburn, A. C., and Semple, S. J. G., Chloramphenicol and Penicillin in the Treatment of Leptospirosis among British Troops in Malaya. *Lancet*, 1:13, 1956.

35. Gochenour, W. S., Jr., Smadel, J. E., Jackson, E. B., Evans, L. B. and Yager, R. H., Leptospiral Etiology of Fort Bragg Fever. *Pub. Hlth. Rpt.*, 67:811, 1952.

36. Adair, C. V., Gauld, R. L., and Smadel, J. E., Aseptic Meningitis a Disease of Diverse Etiology; Clinical and Etiological Studies on 854 Cases. *Am. Internal Med.*, 39:675, 1953.

37. Terzin, A. L., Bordjoski, M. N., Milovanovic, M. V., Stojkovic, L. V., and Dimic, M. M., Some Viral, Rickettsial and Leptospiral Infections Diagnosed in Serbia. A Serological Study. *Jour. Hyg.*, 52:129, 1954.

38. Broom, J. C., Leptospirosis in England and Wales. *Brit. Med. Jour.*, 2:689, 1951.

39. Meyer, Harry M., Jr., Rogers, Nancy G., Miesse, Marie L., and Crawford, Irving P., Aseptic Meningitis Caused by Orphan Viruses and Other Agents. Research Report, Walter Reed Army Institute of Research, Washington 12, D. C., Number 144-56, August, 1956.

40. Wani, H., Uber die Prophylaxe der *Spirochaetosis icterohemorrhagiae durch Schutzimpfung*. *Z. Immunitatsforsch.*, 79:1933.

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Rationale of Vitamin D for Milk Fever

Vitamin D fed in large doses for a few days before the cow calves causes an increase in absorption of calcium from the intestinal tract. This has the effect of maintaining a normal or above normal blood calcium level which helps meet the sudden drain of calcium from the blood into the colostrum. When vitamin D is taken out of the ration effects wear off gradually. This allows parathyroid glands ample time to respond and meet lactation demands through mobilization of calcium from body stores.—*Feedstuffs, Sept. 28, 1957.*

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Single Milk Code Proposed

Under provisions of a bill now before Congress, a single milk code would be established to supercede the present maze of conflicting and duplicating city, county, and state regulations.

The bill sponsored by Representative Lester Johnson (Wisc.) proposes a standard for identity, sanitation and practices in the production, processing, and sale of fluid milk products shipped through interstate commerce.

Laboratory Diagnosis Of Leptospirosis: Demonstration Of Leptospires

WILLIAM S. GOCHENOUR, JR.,* LT. COLONEL, V.C., U. S. ARMY

THE physician or veterinarian seeking laboratory confirmation of the diagnosis of leptospirosis asks that first, his clinical impression be confirmed or negated, second that this information be available as early in the course of the patient's illness as may be possible, and third, that the identity of the infecting leptospire be established as a matter of epidemiologic or epizootiologic interest, and possibly of forensic significance. The demonstration in and recovery of leptospires from appropriate body fluids affords the most definitive confirmation of the diagnosis, is frequently the most rapid laboratory method, and is, in fatal cases, often the only method of establishing leptospirosis.

Theoretically, direct visualization of leptospires in body fluids by darkground illumination affords the most rapid method of laboratory diagnosis. In practice, however, except for the urine of rodents and swine, and the blood of the Syrian hamster, the concentration of leptospires in body fluids is so small as to afford little hope of their successful demonstration. Even more important is the confusion of artefacts such as extrusions from formed blood elements with leptospires. The combination of these two factors is such as to make this procedure, except as noted above, worthless in the laboratory, and to make suspect any diagnosis resting solely on darkground examination for confirmation.

The inoculation of laboratory animals has been widely employed for recovery of leptospires. Most extensively used have been the guinea pig, the Syrian hamster, and the Swiss white mouse. The response of these animals to leptospiral infection varies with the serotype and individual strain of the organism, ranging from inapparent infection to fatal disease, with or without jaundice and with or without massive terminal leptospiremia. For this reason, most leptospiral laboratories today employ guinea pigs or hamsters solely as accelerated living incubators and attempt to demonstrate leptospires microscopically and culturally in either peritoneal fluid or hearts blood of these animals in the first four days postinoculation, rather than to attempt to produce a recognizable illness in the animal. The use of animals has several advantages, first, specimens contaminated with extraneous bacteria and unsuitable for direct culture may be successfully examined. Second, relatively large amounts—several milliliters—may be inoculated into a single animal, and, third the multiplication of the leptospires in the animal may often be so rapid as to permit their microscopic demonstration and thus provide an early positive laboratory diagnosis. Disadvantages are the cost, laboriousness, and hazard of housing and examination of the animals. In addition, many laboratories have encountered *L. ballum* infections naturally occurring in their mouse colonies, which raises the possibility of erroneously reporting a positive diagnosis, due in fact to recovering a leptospire already established in the animal prior to its inoculation with the specimen.

Direct cultivation of aseptically collected specimens, is in our experience the method of choice for the examination of blood and cerebrospinal fluid early in the disease. In comparative studies, direct culture was more efficient in recovery of leptospires from clinical specimens than was animal inoculation. Of the media recommended for leptospiral culture we have found Fletcher's semi-solid and Schüffner's modification of Verwoort's medium most satisfactory. The semi-solid medium has the advantage that growth may be detected macroscopically as a thin white disc approximately two to four centimeters from the surface of the medium, thus saving laborious preliminary darkground examinations during incubation of the cultures. Medium was dispensed in 15-ml. quantities in 30-ml. vaccine bottles with rubber diaphragm stoppers for inoculation by the clinician at the bedside. This proved as satisfactory and efficient as

(Continued on page 570)

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Immunology And Prophylaxis Of Leptospirosis†

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DURING the past several years, there has been a great deal of interest in the problem of leptospirosis. With mounting evidence as to the economic significance of this disease in domestic animals, it is only natural that various prophylactic programs should have been initiated. These remarks are confined to investigations of the problem in the United States, although similar work has been done in other parts of the world.

Prevention and control of leptospirosis depends to a large degree on the background of information on various aspects of the disease accumulated by many research workers. On the basis of this information, it was possible to formulate a prophylactic program. Two approaches were proposed: One involved hygienic measures alone, and the other, hygienic measures coupled with the development of immunity, *i.e.*, vaccination. Prevention by hygienic procedures is possible because of knowledge available on various aspects of the disease, much of which has been discussed by the other speakers at this symposium. However, it is of paramount importance to realize that animals recovered from the infection remain carriers of Leptospira for varying lengths of time. The fact that many animals can experience a subclinical infection without the owner's knowledge is also important. In addition, sylvatic leptospirosis is common, and water contamination can be widespread.

If the disease is actually as sporadic as it appears to be in man in this country, routine hygienic procedures might well be sufficient. Essentially, this means developing methods of making the environment so unfavorable for the leptospiral organism that it does not have a chance to infect man or domestic animals. However, for certain high risk groups such as livestock caretakers, veterinarians, laboratory workers, and certain groups of the armed forces, it might be logical to include vaccination against leptospirosis as part of the program. Vaccination studies in animals, as well as limited human trials in other parts of the world, indicate that this is entirely feasible.

Hygienic procedures could also be incorporated in animal husbandry programs for partial prevention of the disease in various animal groups such as in kennels, dairy and beef herds, and in swine droves. Perhaps the most important step would be to hold all newly purchased or incoming animals in some form of isolation for approximately three weeks prior to introduction into the main herd. This, coupled with serological tests such as described by Stoenner, would at least serve to prevent animals incubating the disease from introducing infection into the herd. The limiting factor in any such program is the lack of practical tests to detect carrier animals. Thus it appears that the only adequate means of prophylaxis for domestic animals is some type of vaccination program.

Research in this country on various types of leptospiral vaccines began a number of years ago. Perhaps the best known early work was by Bruner and Meyer in San Francisco with *L. canicola,* and more recently studies with *L. pomona* by York and Baker. Here again, information acquired in other fields of research was essential in vaccination studies, such as the knowledge that *L. pomona* is the infectious agent for cattle and swine. Data on the course of the disease and its pathology were necessary to properly evaluate any vaccine that might be developed. The fact that cattle could be used in experimental procedures, and that disease could be routinely produced experimentally, was of great assistance in developing and evaluating a vaccine. In cattle, as well as in man and other animals, it was known that recovery from leptospiral infection produced antibodies, and that these persisted for a long period. What was not realized was the significance of a small residual antibody in terms of protection against exposure to virulent Leptospira of the same serotype. We were fortunate in our early work to obtain some cattle that had apparently had a leptospiral infection some time previously, and had

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TABLE 1. Results of Vaccination for Leptospirosis in Experimental Calves

	No. Calves	Pre-Vaccinal C.F.* Test	Post-Vaccinal C.F. Test	Results of Challenge Clinical	C. F. Test
Vaccinated	21	0/21**	0/21	0/21	0/21
Controls	18	0/18	0/18	16/18	18/18

*C. F.—complement-fixation test at a 1:4 dilution of serum.
**Numerator = number of animals showing a reaction; Denominator = number of animals tested.

antibody titers as low as 1:10 to 1:40, based on the agglutination-lysis test. These animals were challenged with virulent strains of Leptospira capable of causing illness in susceptible control animals, and the results revealed that even low titers afforded protection. This indicated that if a vaccine could be developed, the immunity produced would have a protective, and hence practical value even though high antibody titers might not be induced.

Various strains of the organism were employed in the initial studies on *L. pomona* vaccines. One objective was to determine whether one strain was more antigenic than another. The media used in growing the organism were studied in order to find out whether antigenicity could be retained by one type or another. Leptospira were grown initially in various culture media, as well as propagated in the embryonated egg. It now appears, after several years' experience, that the exact manner in which the Leptospira are propagated is not as important as the careful selection of a strain which retains its antigenicity.

I would like to point out that there are a number of other investigators who have also worked with leptospiral vaccines. The tables used in this paper are for the purpose of illustration, and do not necessarily indicate all the work done along these lines in this country. Initially, the vaccine we employed was prepared from egg-propagated Leptospira. The organisms were inactivated by freezing and thawing, and a preservative (usually formaldehyde or merthiolate) added to keep down bacterial contamination. In experimental evaluation of such a vaccine, animals were inoculated with 5 cc. amounts, usually subcutaneously, and after a certain interval were challenged with a virulent strain of *L. pomona*. At the same time, a number of control animals were used to demonstrate that the challenge was actually capable of producing disease. This work is illustrated in table 1. All 21 vaccinated animals in this particular experiment developed immunity and resisted challenge, while 16 of the 18 susceptible controls showed some form of clinical infection, and two died.

The next step in evaluating a vaccine after successful experimental work was to determine how such a product would function in the field where natural exposure would occur. It was not sufficient to know that antibodies could be demonstrated following vaccination. It was important to learn whether vaccinated animals which were exposed to natural infection were actually protected against it. For this reason, vaccination was undertaken in several herds where active leptospiral infection was present. Each of five herds was divided into two groups, consisting of experimental and control cattle. Obviously, a number of the animals vaccinated were going through the incubation stages of the disease during the first three weeks' period. Therefore, in evaluating resistance to infection produced by vaccination, the comparison between vaccinees and controls was begun three weeks after inoculation. This work is summarized in table 2.

A significant difference was noted in the number of new infections occurring in the vaccinated and non-vaccinated cattle in each of the infected herds. This indicated that even under conditions where challenge was present the moment vaccine was inoculated, it was still possible to develop immunity in a significant number of animals, and thus limit the spread of the disease in the vaccinated groups. Details of this field trial have been published elsewhere.

The work so far described concerned the acute phase in which challenge of immunity occurred not later than two months after vaccination. To determine how long this immunity would last required conditions under which the animals would not have an exposure for periods following vaccination. This particular type of study was conducted by Gillespie and Kenzie at Pullman, Wash., details of which are to be published soon. A few summary statements covering this work are pertinent here. In cattle vaccinated as heifers,

satisfactory immunity is present six to eight months after vaccination. A significant number of animals retained immunity for even 15 and 20 months. Thus, for practical purposes, it may be said that immunity lasts for 1½ years.

Vaccination of Swine

Results of vaccination in animals other than cattle are not quite as easy to evaluate, primarily because illness is more difficult to reproduce experimentally. In swine, for example, the chief effect of leptospirosis is the damage to fetuses if the sow is infected during pregnancy. In studies with pigs, 20 animals had an average titer of 1:1800 as determined by the agglutination-lysis test three weeks post-vaccination, indicating that a higher titer can be obtained in swine than in cattle, using the same type of vaccine. There was a marked decline in antibody during the six months following vaccination. However, since the most important period when sows need immunity is during gestation, this antibody protection was considered to be long enough to be of practical value. In studies with pregnant gilts, Bryan found that among non-vaccinated pregnant gilts challenged during mid-gestation, 51% of the pigs born were either dead or in a weakened condition. In contrast, vaccinated gilts produced only 5% dead or weak piglets, demonstrating the value of leptospiral vaccination for swine.

Experiments with horses have been approximately the same. Three to four months after vaccination, antibody titer drops to quite a low level. It is not known whether this particular level will protect horses. Based on work with cattle and swine, it is probably safe to assume that even though antibody titer is low, protection is afforded. Essentially the same results occurred in dogs following use of various *L. canicola* vaccines. Antibody titers dropped to a low level three to four months after vaccination, and it is not known whether protective immunity was present at that time.

Possible Uses for a Leptospirosis Vaccine

1. To check the spread of an infection in a herd.
2. To protect animals in herds adjoining, or downstream from, infected areas.
3. To immunize animals before introduction into known infected herds.
4. In commercial herds, or newly assembled herds.
5. For all animals taken to shows or fairs and returned to the herd.
6. In feeder lots, especially where pigs and cattle are fed together.

Revaccination

The question of revaccination always arises among veterinarians who are faced with leptospiral infection. How important it is to revaccinate a group of animals must be determined by what is known about the disease and the situation at the time. In general, until further experience is available, it is probably necessary to revaccinate sows before every breeding season. In cattle, as indicated, additional antibody stimulus may be needed after a year or 18 months. Numerous studies now indicate that leptospirosis is widespread in cattle and swine. Veterinarians and livestock owners have become increasingly aware of the importance of this disease. During the past 2½ years, about 1,500,000 cattle and swine have been vaccinated with *L. pomona* vaccine. A number of different situations call for the use of such a vaccine. Table 3 covers various conditions where vaccination may be used most effectively, and be of practical value.

Certainly one can not say that we have the

(Continued on page 570)

TABLE 2. Summary of Results of Serological Studies in *L. pomona* Field Trial Herds

Herd	Vaccinated Cattle	Control Cattle	Results							
			Prevac. Reactors		3 wk. Reactors		6 wk. Reactors		% Neg. at 3 wk. Reacting at 6 wk.	
			V	C	V	C	V	C	V	C
Alberson	91	39	19	7	38 (20n)*	13 (8n)	22 (3n)	15 (5n)	5.8	21.0
Bivens	71	29	13	5	15 (6n)	5	7	5 (2n)	0	8.3
Langley	25	13	4	2	6	3	6	8	0	60.0
Elmes	50	43	—	—	1	1	2 (1n)	6 (5n)	2.0	11.9
Elmes	40	28	1	1	5 (5n)	1	4 (1n)	4 (4n)	2.8	14.8

V=vaccinated cattle; C=control cattle; *n=new.

The Treatment of Leptospirosis in Man†

JOE L. STOCKARD,* M.D., Baltimore, Maryland

PRIOR to the introduction of antibiotic agents, many forms of therapy were employed in the treatment of leptospiral infections in man. Among these, arsenical and bismuth preparations were used extensively but failed to give consistently satisfactory results.[1] Gsell[2] has attributed some value to the early administration of type specific hyperimmune serum, but this is limited because proper diagnosis often can not be established early in the illness and the causative leptospire can not be identified promptly. Sulfonamides have been shown devoid of therapeutic value.[3]

The effects of several antibiotics on leptospires *in vitro* and *in vivo* have been studied by a number of investigators.

Penicillin

Alston and Broom[4] found growth of *Leptospira icterohemorrhagiae* and *L. canicola* suppressed by penicillin in concentrations of 0.11 Oxford units per milliliter when tested under *in vitro* conditions. Lower concentrations of the antibiotic produced variable results. Chang's[5] studies revealed that penicillin inhibited multiplication of *L. icterohemorrhagiae* in tap water and culture media but exposure of the leptospires to 5,000 units per ml. of this drug failed to produce a leptospirocidal effect.

Several groups of investigators reported that penicillin protected experimental animals infected with virulent leptospires. Heilman and Herrell[6] tested this drug in 32 treated and 32 untreated guinea pigs inoculated with *L. icterohemorrhagiae*. Therapy with 800 Oxford units of penicillin daily for seven days was begun from 17 to 24 hours after the animals were infected. Of the untreated group, 29 died and all presented the typical pathologic lesions associated with leptospirosis. All but three of the treated animals survived and none of the entire group showed lesions of leptospirosis at autopsy.

Augustine, Weinman and McAllister[7] found penicillin ineffective in either treating or protecting guinea pigs infected with *L. icterohemorrhagiae* when the delay between inoculation and initiation of treatment exceeded 38 hours. Chang[5] demonstrated disappearance of leptospiremia within three to five days after inoculation when the serum level of penicillin was maintained at 0.4 units but, he and other investigators[5,7,8] recovered viable organisms from tissues of animals some of which were treated with even larger amounts of this drug. Chang and Alston and Broom[5,4] found rising titers of agglutination-lysis antibodies to the infecting leptospire in animals which survived on penicillin treatment.

Streptomycin

In 1945, Heilman[9] reported results of controlled experiments in which treated animals received streptomycin beginning 17 hours following inoculation of virulent *L. icterohemorrhagiae*. Streptomycin was given to 25 hamsters in the dosage of 1000 units daily for ten days. All of these animals survived and were sacrificed on either the 28th or 33rd post-inoculation day. The 25 untreated animals died prior to the tenth day of infection and presented typical pathologic lesions of leptospirosis. Liver and kidney tissue from 16 of the treated hamsters was emulsified and guinea pigs inoculated with suspension of this material. Leptospires were not recovered by this method.

Brunner and Meyer[10] found streptomycin effective in eliminating the carrier state in dogs and hamsters shedding *L. canicola* in their urine. Penicillin was without value in either preventing or treating this complication.

Broad Spectrum Antibiotics

Schlipköter[11] noted *in vitro* variation in the susceptibility of six species of leptospires to terramycin,®[1] aureomycin,®[2] streptomycin and chloramphenicol (chloromycetin)®[3]. Of these, terramycin was most effective, and chloramphenicol, the least active. Leptospirostatic ef-

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®[1]Chas. Pfizer Co., Brooklyn, N. Y.

®[2]American Cyanamide Co., Pearl River, N. Y.

®[3]Park, Davis Co., Detroit, Mich.

fects were produced by these drugs in concentrations readily attainable in the blood of man but bactericidal action required quantities exceeding the levels ordinarily achieved in patients.

Brunner and Meyer[13] observed that aureomycin protected animals inoculated with *L. canicola* and furthermore found this drug capable of preventing or eliminating the carrier state.

Uhlenhuth and Schoenherr[13] considered terramycin more efficient than aureomycin in treating hamsters infected with *L. canicola.* They were unable to recover viable leptospires from the tissue of terramycin treated animals.

Dunn and Thompson[14] found chloramphenicol totally ineffective in controlling growth of *L. icterohemorrhagiae in vitro,* in protecting hamsters or guinea pigs inoculated with virulent leptospires, or in preventing development of the carrier state in dogs.

Chemotherapy in Leptospiral Infections Of Man

According to the criteria employed by Smadel[15] effective therapeutic agents should possess the following properties for successful treatment of infectious diseases: (1) Render the patient afebrile and atoxic within a reasonable period, even when administered relatively late in the disease, (2) inhibit promptly the multiplication of the infecting agent and contribute to its disappearance from the body within a reasonable number of hours, (3) reduce or eliminate the complications ordinarily associated with the disease, including the carrier state if it occurs, (4) possess activity against all strains of the organism in a given geographic area, and (5) be relatively safe, simple, and inexpensive to use. This investigator notes also that some drugs, although useful, lack one or more of the above features.

An effective drug is recognized readily as one fulfilling these criteria when it alters the usual course followed by a disease which is uniform in duration, severity, and prognosis. These features vary in the human leptospiroses; hence, the efficacy of treatment is difficult to assess.

In several early reports dealing with single cases or small outbreaks of leptospirosis, opinions differed regarding the value of chemotherapy.[16,17,18,19]

In 1951, Hall *et al*[20] tested five antibiotics in the treatment of human leptospiral infections in Puerto Rico. This diagnosis was confirmed in 79 patients by isolation of leptospires from blood, urine or spinal fluid, by detection of rising titers of specific antibodies, or by both procedures. About two thirds of the cases suffered an illness caused by *L. icterohemorrhagiae,* while the remainder were caused by organisms of the *L. bataviae, L. ballum, L. hebdomadis,* and *L. pyrogenes* serogroups. Antibiotics were administered to 67 patients divided into the following therapeutic groups: 24 treated with aureomycin, eight with teramycin, 18 with chloramphenicol, 12 with streptomycin, and five with penicillin. Of the 24 patients treated with aureomycin, 13 received this antibiotic alone, nine were given streptomycin and aureomycin concurrently and two severely ill patients received cortisone and aureomycin simultaneously. No chemotherapy was given to 12 additional patients who served as controls. Criteria for estimating severity of illness were based upon the duration and severity of specific physical signs and laboratory procedures which included uninalysis, blood urea nitrogen determinations, and liver function studies.

Only two of the 79 patients succumbed. One died on the seventh day of disease four hours after receiving the first dose of aureomycin and cortisone. The second fatality was a chronic alcoholic male who expired on the seventh consecutive day of chloramphenicol therapy, which was the 12th day of disease.

The mean duration of fever was 9.2 days in the treated groups as compared with 8.6 days in those who received no antibiotics. Icterus was not observed in the untreated cases but clinical overt jaundice appeared in 28 patients, which were distributed about equally, among the groups receiving different antibiotics. In 18 instances, icterus either developed or increased after chemotherapy was initiated. Blood urea nitrogen values varied from 12.3 to 117 mg. per cent in the treated cases, five of whom developed uremia. In the untreated group elevated blood urea nitrogen values and uremia were not observed. Among the 29 patients with leptospiremia when antibiotic therapy began, 16 still had the organism in their blood on the following day and in one instance leptospires were isolated from the blood on the 12th day of penicillin therapy.

These investigators concluded that none of the antibiotics employed was effective in the treatment of leptospiral infections in man.

Fairburn and Semple[21] employed penicillin and chloramphenicol in the treatment of patients suffering with milder forms of leptospirosis in Malaya. In this study, patients with fever were included if symptoms and

signs suggested leptospirosis to be the likely diagnosis. Selected cases received, in rotation, chloramphenicol 500 mg. every six hours (31 patients), penicillin 600,000 units every six hours (21 patients) or no chemotherapy (31 patients. Experimental medications were discontinued after the oral temperature had been normal for 24 hours. Comparison of the groups with regard to duration and height of fever and clinical manifestations revealed no significant disparity. Pyrexia reappeared after temperature had been normal for 48 or more hours in six of the control patients as compared with three who received chloramphenicol and three treated with penicillin. Disturbed renal function evidenced by oliguria was noted once in each treated group and twice in the controls. Neither drug demonstrated any appreciable effect on the development or progression of either azotemia or jaundice. These investigators concluded that the two experimental drugs possessed little if any beneficial effect in the treatment of the milder forms of leptospirosis encountered in Malaya.

Gsell[22] has observed the effect of early antibiotic therapy of leptospirosis in an area where benign non-icteric forms of the disease prevail. Without specific medications fever always persists over six days, spinal fluid becomes abnormal during the second week and elevation of temperature recurs after the eight day of disease with astounding regularity. These features were observed in all of 50 patients who received no chemotherapy. In three instances initial doses of aureomycin or terramycin were given on the second day of disease. None of these patients developed serious meningitis or experienced a recurrence of pyrexia and the total duration of fever was less than seven days. When, in seven additional cases, administration of these antibiotics was delayed until the third or fourth days after onset, only secondary fever was prevented. The usual progression of the disease was unaltered if treatment was delayed beyond the fourth day of illness. Neither penicillin nor chloramphenicol exhibited these therapeutic properties.

A second interesting observation made by Gsell is related to antibody formation. One-half of the ten patients who received chemotherapy between the second and fourth days of disease, developed low agglutination lysis titers ranging from 1:100 to 1:1000. When treatment was initiated after the fourth day only one of 14 patients developed a titer less than 1:1000. Likewise, none of the cases treated early produced titers in excess of 1:8000, while one third of those treated late in the febrile phase had high titers.

Doherty[23] has studied the effect of penicillin and three broad-spectrum antibiotics in 273 cases of mild leptospirosis in Australia. Diagnosis was confirmed by accepted laboratory methods in all cases and 13 different serotypes of leptospires were represented. Of these 85 were caused by *L. australis A* and 69 were due to *L. australis B*, while each of the remaining organisms produced relatively few cases. Penicillin was administered in doses of 800,000 units, 1,000,000 to 3,000,000 units or 4,000,000 units daily to 181 patients. Two additional groups, including 26 and 37 cases each, received either tetracycline, oxytetracycline, or chloramphenicol alone or with penicillin. No specific therapy was given to 20 patients in whom the diagnosis was not suspected initially because of the mild nature of the disease.

There were no deaths and in general all patients experienced a mild illness. One individual developed uremia but recovered without chemotherapy. Uremia occurred in only one other patient who was also the only patient to develop evident jaundice. In this instance penicillin and terramycin were given concurrently from the 10th to 19th days of disease and though gradual improvement was noted the value of the antibiotics remains questionable. Uveitis appeared in four patients treated with penicillin in dosages varying from 800,000 to 4,000,000 units daily and in one patient who received no antibiotic. No attempt was made to evaluate the effect of the experimental drugs on clinical manifestations, leptospiremia, or abnormalities associated with renal, hepatic, and cardiovascular decompensation. The various groups were analysed only as regarded duration of pyrexia. In general, patients who received penicillin experienced a shorter febrile period and those who received large doses of this drug recovered faster than those who received small doses. The broad-spectrum antibiotics were less effective than penicillin in reducing the duration of fever.

The time of inoculation with virulent leptospires is seldom known in man, except in those rare instances when infection is acquired in the laboratory. Broom[24] observed a laboratory infection in a worker inoculated by a needle, contaminated with leptospires of the *L. javanica* serogroup, which pierced the skin over the dorsum of the foot. Alcohol was applied to the wound immediately after the accident and within an hour 1,000,000 units of penicillin was administered by mouth. Treatment with this drug was continued in a dosage of

500,000 units every six hours for a total of 6,000,000 units. Fever, malaise, headache, retro-orbital pain, and stiffness of the neck developed ten days after inoculation. Therapy with terramycin, 250 mg. every six hours, was initiated on the first febrile day. The duration of the illness was about three days following which the fever and other clinical manifestations abated fully.

Cultures of blood yielded a leptospire indistinguishable immunologically from the strain under study in the laboratory.

The initiation of penicillin therapy within minutes after infection occurred failed to prevent the subsequent development of clinical manifestations of acute leptospirosis. Furthermore, there is little evidence that early administration of this antibiotic, in the relatively low dosage employed, delayed the onset of disease.

Apparently none of the available antibiotics can alter the course of human leptospiral infections. Treatment with massive doses of penicillin merits continued study particularly in the severely ill patients in whom reliable data may be obtained. Duration of fever alone is not a reliable criterion to employ in evaluating effectiveness of a chemotherapeutic agent.

General Supportive Measures

In the absence of highly effective specific therapy, general supportive measures are extremely important, particularly in caring for the severely ill. Admission to hospital is desirable in such cases especially if jaundice is present. Bed rest should be maintained until the fever subsides. Pain may be alleviated by the judicious use of codeine or salicylates but the latter should be avoided in the presence of hemorrhagic manifestations. Modest doses of barbiturates may be given for sedation but use of these and the opiates is dangerous in patients with jaundice. Severe protracted vomiting can best be controlled by curtailing all oral alimentations. Provision of a high carbohydrate, high protein, high vitamin intake is essential. When necessary, these may be administered parenterally. Careful attention must be given to fluid and electrolyte balance particularly during the second week of disease when renal insufficiency may develop and in the diuretic phase which follows. During this critical period frequent determinations of serum sodium, K, Cl, CO_2 combining power and blood urea nitrogen (BUN) are helpful in directing therapy. Other biochemical tests of value in following progression of the illness include the van den Bergh reaction, thymol turbidity total, and fractional proteins. The patient may develop oliguria or anuria and under such conditions management should be similar to that given patients with lesions of the lower nephron type.

Good nursing care is vitally important. The nurse, should promptly report marked variation in blood pressure or pulse rate, the occurrence of dyspnea and hemorrhage from any source. Frequent turning of the patient may help prevent pulmonary complications. Abdominal distention may be relieved by insertion of a rectal tube or by administration of enemas. Strong cathartics may induce bleeding and should therefore be avoided. Since excreta often contain leptospires, urine and feces should be sterilized before disposal. Spinal fluid also contains viable organisms and should be handled with caution.

Conclusions

1. Chemotherapeutic agents now in general use have been shown in laboratory studies to possess leptospirostatic properties in concentrations easily attainable in the blood of patients.

2. Penicillin, streptomycin, aureomycin, and terramycin protect laboratory animals infected with virulent leptospires when treatment is begun shortly after inoculation but are of little if any value after jaundice appears. Chloramphenicol possesses no protective or therapeutic effect.

3. Viable leptospires can be recovered from tissues of animals treated with penicillin but not from those given streptomycin, aureomycin or terramycin. Streptomycin and aureomycin can prevent or eliminate the carrier state in animals.

4. Leptospires of different serogroups vary in their susceptibility to antibiotics.

5. Penicillin administered in doses of 4,000,000 units daily appears to shorten the duration of fever in some mild varieties of human leptospirosis but even in these large doses does not prevent ocular complications.

6. None of the chemotherapeutic agents have been shown conclusively to influence significantly the course of human leptospirosis when administered after the onset of renal, hepatic, or vascular decompensation.

7. Careful attention to general supportive measures is of paramount importance in treating patients seriously ill with leptospirosis.

REFERENCES

1. Walch-Sorgdrager, B., Leptospiroses. *Bul. Health Org.*, League of Nations, 8:143, 1939.

2. Gsell, O., Leptospiroses, Bern, Medizinischer Verlag Hans Huber, 1952.

3. Patterson, H. M., Weil's Disease—Observations in 61 cases with Special Reference to the use of Penicillin in 6 cases. *Jour. Am. Med. Assn.*, 134:1077, 1947.

4. Alston, J. M., and Broom, J. C., The Action of Penicillin on Leptospira and on Leptospiral Infections in Guinea Pigs. *Brit. Med. Jour.*, 2:718, 1944.

5. Chang, S. L., Studies on *Leptospira icterohemorrhagiae*. II. A Critical Study of the Effect of Penicillin on *Leptospira icterohemorrhagiae in vitro* and in Guinea Pigs. *Jour. Clin. Invest.*, 25:752, 1946.

6. Heilman, F. R., and Herrell, W. E., Penicillin in the Treatment of Experimental Relapsing Fever. Proc. Staff Meet., Mayo Clinic, 18:457, 1943.

7. Augustine, D. L., Weinman, D., and McAllister, J., Penicillin Sodium Therapy in Experimental Weil's Disease. *New Eng. Jour. Med.*, 231:358, 1944.

8. Borg-Peterson, C. B., and Schmidt, M. R., Effect of Penicillin on Leptospirae *in vitro* and on Leptospirosis in Guinea Pigs. *Acta path. et microbiol., Scandinav.*, 22:462, 1945.

9. Heilman, F. R., Streptomycin in the Treatment of Experimental Relapsing Fever and *Leptospirosis icterohemorrhagiae* (Weil's Disease). Proc. Staff Meet., Mayo Clin., 20:169, 1945.

10. Brunner, K. T., and Meyer, K. F., Streptomycin in the Treatment of Leptospira Carriers. Experiments with Hamsters and Dogs. *Proc. Soc. Exper. Biol. and Med.*, 70:450, 1949.

11. Schlipkoter, H. W., Ein Beitrag zur Therapie der Leptospirosen. *Munch. Med. Wschr.*, 93:2300, 1951.

12. Brunner, K. T., and Meyer, K. F., Effects of Aureomycin on *Leptospira canicola* and *Leptospira icterohemorrhagiae in vitro* and Experimental Carrier Studies. *Am. Jour. Vet. Res.*, 11:89, 1950.

13. Uhlenhuth, P., and Schoenherr, K. E., Tierexperimentille Untersuchungen uber die Therapie der Leptospirosen. *Med. Klin.*, 32:859, 1951.

14. Dunn, M. C., Thompson, P. E., Chemotherapy of Experimental Leptospirosis with Chloramphenicol (chloromycetin), Subtilin and Penicillin G. *Jour. Inf. Dis.*, 92:1 (Jan.-Feb.), 1953.

15. Smadel, J. E., Symposium on the Leptospiroses: The Therapy of Leptospirosis. Army Medical Service Graduate School, Medical Science Publication, no. 1: p. 203, 1952.

16. Blumer, E., Weil's Disease in Normandy: Its Treatment with Penicillin. *Brit. Med. Jour.*, 1:113, 1945.

17. Suchett-Kaye, A. I., Penicillin in Weil's disease. *Lancet*, 1:90, 1951.

18. Brainerd, H. D., Lennette, E. H., Meiklejohn, G., Bruyn, N. B., Jr., and Clark, W. H., Symposium on Antibiotics: The Clinical Evaluation of Aureomycin. *Jour. Clin. Invest.*, 28:992, 1949.

19. Batchelor, T. M., and Todd, G. M., Aureomycin and Penicillin Therapy in Leptospirosis (Weil's Disease). *Jour. Am. Med. Assn.*, 1950.

20. Hall, H. E., Hightower, J. A., Diaz Rivera, R., Byrne, R. J., Smadel, J. E., and Woodward, T. E., Evaluation of Antibiotic Therapy in Human Leptospirosis. *Ann. Int. Med.*, 35:981, 1951.

21. Fairburn, A. C., and Semple, S. J. G., Chloramphenicol and Penicillin in the Treatment of Leptospirosis among British Troops in Malaya. *Lancet*, 1:13, 1956.

22. Gsell, O., Symposium on the Leptospiroses: Treatment of Leptospirosis. Army Medical Service Graduate School, Medical Science Publication, no. 1:212, 1952.

23. Doherty, R. L., Further Observations on the Treatment of Leptospirosis. *Australian Ann. of Med.*, 5:23, 1956.

24. Broom, J. C., Norris, T. St. M., Failure of Prophylactic Oral Penicillin to Inhibit a Human Laboratory Case of Leptospirosis. *Lancet*, 1:721, (Apr. 6), 1957.

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Laboratory Diagnosis

(Continued from page 562)

cultures made in the laboratory from glass-bead defibrinated blood. In our experience, inoculation of minimal quantities, 1 - 2 drops, in each of several tubes of medium resulted in successful isolation in one or more of the tubes, whereas, the inoculation of larger quantities was uniformly unsuccessful. Advantages of direct cultural examination of appropriate specimens are, first, cost, hazard and laboriousness are less than with any other technic, second confirmation of the clinical diagnosis may often be made within the first week of incubation of the culture. Disadvantages are unsuitability for examination of specimens contaminated with extraneous bacteria and second, the requirement for prolonged incubation, at least four weeks, before cultures may be safely discarded as negative.

Identification of the leptospires recovered can be definitively accomplished only at leptospiral reference laboratories equipped to perform the agglutinin-absorption studies required. The Veterinary Division, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, has been designated by the World Health Organization, with the concurrence of the Surgeon General, U. S. Public Health Service and The Surgeon General, U. S. Army, as the Leptospiral Reference Laboratory for North America.

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Immunology and Prophylaxis

(Continued from page 565)

final answer as far as vaccines are concerned. We would like to have one that produces a much longer immunity, and that produces immunity more rapidly. We must be constantly aware that new serotypes other than *L. pomona* may occur in domestic animals, and would have to be included in a vaccine if they became important. A distinct possibility is the development of a modified, or avirulent, strain of leptospirosis which could be incorporated into a vaccine. This type of product might create a stronger or more rapid immunity than the present killed vaccines.

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Just Dreams!

I was lying in the porch swing after having a meal of Welch rabbit when:

1. The dairy farmer said to me, "Doctor, let me pay you now so you will not have to send a bill."

2. The repair man brought back my electric clippers and said, "Just a loose wire — no charge!"

3. The Humane Society president phoned and told me, "You know more about this than we do, so what ever you say goes!"

4. The beautiful blond client was telling me about her cat troubles when my wife came by and smiled and said, "Dear, why don't you show the young lady your coin collection?"

5. The community sales office announced, "Any animal the doctor says is not perfectly healthy will not be sold."

6. A farmer told me, "I never treat my animals as I figure it is cheaper in the long run to call you."

I think I have the craziest dreams!—*E. J. F.*

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STREPTOKINASE—HUMAN PLASMINOGEN—STREPTODORNASE

Removes the disease barrier

Parenterally: The "disease barrier" has been a formidable barrier blocking the admission of oxygen, humoral agents and antibiotics.

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Recoveries attributed to VARIZYME have been in mammary edema, cellulitis, acute clinical mastitis, mandibular phlegmon, trauma, feline chronic cough, metritis and dermatitis.

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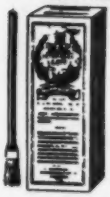

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Storm Losses

In addition to huge toll in lives and property, severe storms cause losses in livestock frequently unnoticed because of the extent of human suffering. An estimate places losses caused by hurricane Audrey, which struck Louisiana in June, at 29,500 cattle.

▾ ▾ ▾

Official pig crop estimates indicate near 10% increase of spring pigs in 1958 over the number farrowed in 1957.

New Director of Research—Jensen-Salsbery Laboratories

Jensen-Salsbery Laboratories have announced appointment of Dr. S. K. Sinha as director of research.

Dr. S. K. Sinha

Doctor Sinha is a graduate in veterinary medicine from the University of the Philippines and obtained his master's and doctorate degrees in virology at the Department of Veterinary Science, University of Wisconsin.

Prior to his association with Jen-Sal, he directed the A.R.S. Regional Diagnostic Laboratory at Philadelphia, then served an assistant professorship at the University of Pennsylvania. Later he was associated with tissue culture research on human coryza viruses.

▾ ▾ ▾

Scholarship for M. S. U.

A $5,000. scholarship fund for students of veterinary medicine at Michigan State University has been accepted.

The fund is a gift from Mrs. Georgia E. Corbin of Grand Rapids in memory of her son, Dr. Gail E. Hawley, a 1950 graduate of the M.S.U. College of Veterinary Medicine. Doctor Hawley died March 16, 1957.

The scholarship, to be awarded from the fund will be known as the Dr. Gail E. Hawley Scholarship, and will consist of $500. each year to a student in the fourth year of study in the College of Veterinary Medicine.

To qualify for the scholarship, students must be above average in scholarship, have financial need and give promise of making a contribution to the profession of veterinary medicine.

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Court Decision Concerning So-called "Trained Technicians"

The Asociacion Médico-Veterinaria de Puerto Rico (Puerto Rico Veterinary Medical Association), a constituent of the American Veterinary Medical Association, has received a favorable decision from Superior Court Judge Rafael L. Ydrach-Yordan on legal action brought against Luis Rivera-Santos, Secretary of Agriculture of Puerto Rico, relative to the use of laymen or so-called "trained technicians" in venipuncture in the accelerated brucellosis eradication program carried on the Island as a state-federal cooperative endeavor.

Judge Ydrach concluded civil case no. 56-4373 on July 15, 1957, a hearing having been held on January 22, stating that:

(a) Only a technician duly authorized by the Puerto Rico Board of Veterinary Examiners can draw blood samples from cattle for brucellosis testing;

(b) being an operation that needs specialized technical knowledge *per se* and for the attention and treatment of possible pathological complications, such as, hematomas, phlebitis, heart-block, septicemia, embolism, pulmonary edema-that might ensue and that may even be causative of the animal's death, venipuncture, being a phase of the practice of veterinary medicine and surgery must be preformed by experts, compliant to the practice of veterinary science as authorized and regulated by the only organism that, under the law, has been empowered to do so, *i.e.*, the Puerto Rico Board of Veterinary Examiners;

(c) the Secretary of Agriculture of Puerto Rico has gone beyond his attributes in creating the post of so-called "trained technicians" (laymen-bleeders);

(d) this action of the Secretary of Agriculture of Puerto Rico is unlawful and beyond the scope or range of his faculties.

As the Practice Act of Puerto Rico refers only to, and exclusively to, graduates from accredited veterinary schools, it necessarily follows that the terms "technicians" and "experts" as used by Judge Ydrach refer to licensed veterinarians, graduated from accredited schools.

It should be stressed that, among the administrative steps taken unfruitfully by this P.R.V.M.A. in trying to persuade the Secretary of Agriculture of Puerto Rico to desist from violating the law, and twisting regulations to make them meet his criterion, was the objective of resolutions from the Puerto Rico Board of Veterinary Examiners in March 1955, and again in March 1956 to the effect that venipuncture is a veterinary surgical intervention and therefore, "laymen-bleeding" was unlawful in Puerto Rico.

In that same direction, the House of Representatives of the A.V.M.A. carried a motion or resolution at its San Antonio meeting in October 1956 to the effect of withdrawing the A.V.M.A.'s support to regulatory programs as carried out where laymen were being used over and against the manifest objection and disapproval of the local constituent veterinary association concerned, as was the case of the P.R.V.M.A. in this instance.

We consider the court ruling of basic, elementary importance in upholding the rights and principles of sane scientific professional veterinary deportment here in Puerto Rico. Probability of application elsewhere where unlawful laymen-bleeding is being officially patronized by governmental agencies might be worth considering.—*José D. Rivera-Anaya, V.M.D., Secretary, Puerto Rico Veterinary Medical Association.*

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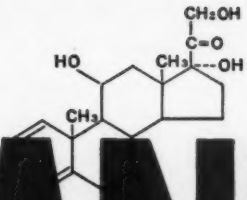

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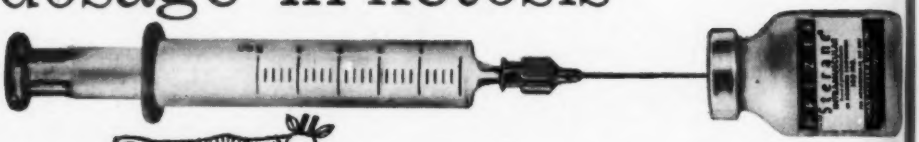

...87% of cases of primary ketosis cured with a single injection of only 50 to 100 mg. of Sterane Intramuscular

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*Link, R. P.; Newton, D. I., and Huber, W. G.: The Use of Prednisolone in Bovine Ketosis, paper presented at the 93rd Annual Meeting, A.V.M.A., San Antonio, Texas, Oct. 15-18, 1956.

Pfizer *Department of Veterinary Medicine*
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Doctor Adler Cited for Newman Award

Dr. Henry E. Adler, WSC '46, poultry pathologist of the School of Veterinary Medicine, University of California, Davis, was presented the Newman International Poultry Award for 1957, according to release by the California school.

Dr. Henry E. Adler

The Award, consisting of a medal and money prize, was instituted nine years ago by the Poultry Association of Great Britian. It has been won six times by United States scientists, including veterinarians Ben R. Burmester, Henry Van Roekel, and Fred R. Beaudette.

Doctor Adler's contributions to the knowledge of poultry diseases was cited by the Award Committee. Mentioned was his work on complex infections caused by pleuropneumonia-like (PPLO) organisms complicating chronic respiratory disease in chickens and infectious sinusitis in turkeys.

▼ ▼ ▼

Photograph Foot-and-Mouth Disease Virus

An electron micrograph has been made of foot-and-mouth disease virus by scientists of the Plum Island laboratories.

Foot-and-mouth disease virus has been known to be small. These studies indicate it to be round and approximately 1/1,000,000 in. in diameter. This and continued basic studies on the character of the viral agent of this disease is expected to advance research effort to develope more effective means of prevention and control.

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Sample containers and price list on request.

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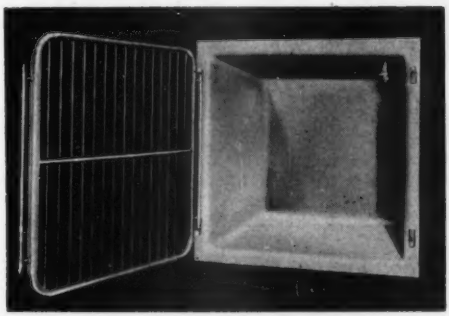

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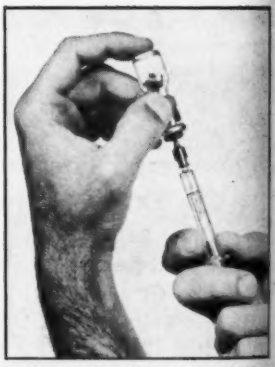

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Preliminary data point to new indications for FURADANTIN. Various reports describe encouraging results with FURADANTIN in the treatment of vaginitis in the bitch and genitourinary tract infections of mares.[2] Another article concludes that FURADANTIN is an excellent adjunct to surgery in the treatment of prostatic abscess in the dog.[3]

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Available as orange scored tablets of 10, 50 and 100 mg.; and Oral Suspension, bottle of 60 cc.

REFERENCES: 1. Mosier, J. E.: Vet. M. 50:605 (Nov.) 1955. 2. Belloff, G. B.: Calif. Vet. 9:27 (Sept.-Oct.) 1956. 3. Pollock, S.: J. Am. Vet. M. Ass. 129:274 (Sept.) 1956.

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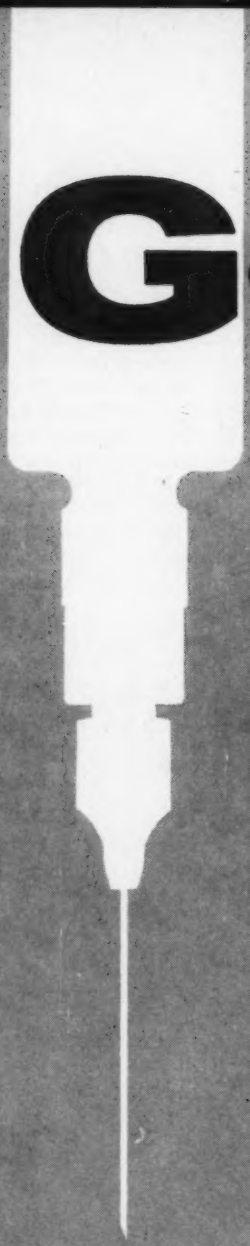

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Supplied: 30-cc. multidose vials, each cc. containing 50 mg. of Gallogen.*

Dosage: Intramuscular or intravenous administration. Cattle—500 mg. (10 cc.) Sheep and Swine—200 mg. (4 cc.) Dogs and Cats—50 mg. to 100 mg. (1 cc. to 2 cc.)

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Georgia Association Honors Dr. W. F. McLendon

Presentation of the Georgia Veterinarian of the Year Award to Dr. W. F. McLendon highlighted convention activities of the June Georgia meeting held at the Continuing Education Center, University of Georgia, Athens, on June 23-25, 1957.

Contributors to the literary program included Drs. M. G. Fincher, W. W. Armistead, R. J. Anderson, Jack Knappenberger, T. L. Steenerson, and Douglas Watson.

Officers elected for the ensuing year were Dr. L. A. Mosher, Atlanta, president; Dr. Wa. Elinburg Jr., Lawrenceville, president-elect; and Dr. A. M. Mills, Athens, secretary-treas.-editor.

The Associations of Georgia and South Carolina now plan a joint annual meeting for 1958.

▼ ▼ ▼

Iowa is accepting registrations for hygromycin, an antibiotic claimed to have superior anthelmintic properties, to be added to bagged feed for swine. Feed products must contain 0.006 gm. hygromycin per pound.

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The most convenient oral aid in intoxications of obscure alimentary origin, often accompanying milk fever, acetonemia and other morbid conditions (downers) in which there is reduced or impaired intestinal motility.
The toxopexic action of **ALKADOTE** acts to fix certain toxins and other harmful substances in the alimentary tract, rendering them harmless to the animal, until they can be removed by a laxative, such as **BOVIDOTE, PURGICIN** or **PERI-LAXIN.**
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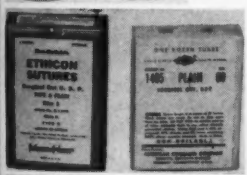

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Dr. Alvin A. Price Appointed New Dean at Texas

Dr. Alvin A. Price, a 39-year-old assistant professor of veterinary anatomy was named on August 23, as the new dean of the School of Veterinary Medicine at the A. and M. College of Texas. His election by the A. and M. System Board of Directors was upon recommendation of the president of A. and M. College, with approval of Chancellor M. T. Harrington.

Dr. Alvin A. Price

The promising young scientist and administrator who was chosen from the ranks to head one of the 17 accredited schools of veterinary medicine in the nation, made a slow start in his chosen field. He first attended Tarleton State College at Stephenville, where he graduated in 1938, then Texas A. and M. where he took his B.S. degree in 1940 in the field of dairy husbandry. He worked in this field at a Lockhart (Texas) creamery from graduation until he entered the Army in 1942.

War Service

After serving as an infantry company commander in the African, European and Middle Eastern areas, where he earned six citations and was promoted to battalion commander, Doctor Price returned to A. and M. College as a veteran student in 1946 and enrolled in the School of Veterinary Medicine. He took his D.V.M. degree in 1949 and stayed on at A. and M. College as an instructor in veterinary anatomy, working meanwhile on his M.S. degree in veterinary physiology, which he received in 1956.

Dean Price has crowded an amazing amount of professional activity into the eight years since he received his veterinary degree. He

served as acting head of the Veterinary Anatomy Department in 1950, was a delegate to the House of Representatives of the American Veterinary Medical Association in 1952-53, while serving also as executive secretary and editor for the Texas Veterinary Medical Association. He was president of the Texas Association in 1956 and is president of the American Association of Veterinary Anatomists (1957-1958). He has also served during this time as president of the Phi Zeta and Phi Kappa Phi honorary fraternities at A. and M. College.

A native of Dublin, Texas, Dean Price is married and has two children. Their home is at 1203 Walton Drive, College Station.

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Anti-Inflammatory Properties of Organic Iodide

A progress report published in the current (Sept. 1957) issue of *The Jen-Sal Journal* establishes a previously unknown therapeutic activity for cuprous iodide (paladide® Jen-Sal).

Observations of the anti-inflammatory properties of the specific organic iodide were made on routine investigational work employing the granuloma pouch technic developed by Hans Selye. It has been shown that cuprous iodide orally in rats (100 mg./kg.) was more effective anti-inflammatory agent than 10 mg./kg. of cortisone acetate injected subcutaneously.

The establishment of this property suggests its broadened use in many inflammatory conditions including foot rot, keratosis, wound infections, dermatitis, and others.

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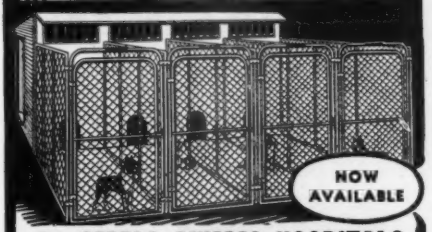

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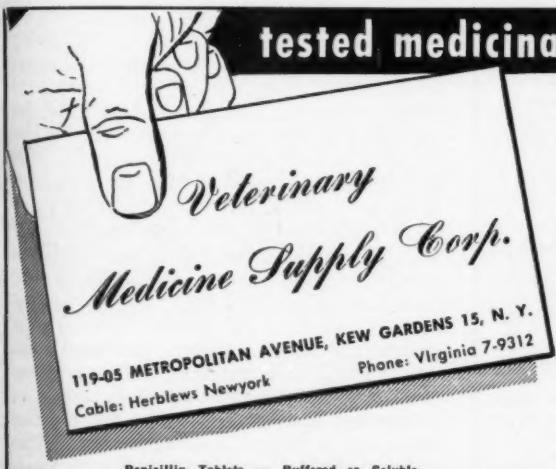

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100 tablets, 500,000 units each (500 tabs. 28.00)	(Buffered only)	6.00
100 Penicillin, 100,000 units with Triple Sulfa (500 tabs. 20.00)		4.50
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Penicillin G Procaine in Aqueous Suspension or Oil
300,000 Units cc 10cc Vial
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1 Vial .75c
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Tetracycline HCL 250MG — Caps. (Nationally known brand) 100's 22.49
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GREAT HEAT and FIREPOWER — 125,000 BTU. HYDRAULIC REFRACTORY CONCRETE 1½" insulation.

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CAPACITY 8-BUSHEL — FEED DOOR 21" W x 19" H.

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100% SAFETY AUTOMATIC MR2 THERMOPILOT VALVE pilot light burner — main burner pressure type. Automatic timer shut-off control. Barometric Damper.

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MANY ANIMAL HOSPITALS USING THIS EQUIPMENT. Fully equipped. shipped assembled. simple to install. Bolted construction. Portable. Compact. Wgt. over 800#.

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LARGER CAPACITIES ARE AVAILABLE IF REQUIRED

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Investigate unique purchase plan for great saving to D.V.M. or kennel owner.

Syrall Manufacturing Company

511 North State Street, Syracuse 3, N. Y.

First Chief of Air Force Veterinary Services is Decorated and Retired

Brigadier General Wayne O. Kester, U.S.A.F. (VC), first assistant for Veterinary Services to the U.S.A.F. Surgeon General is shown receiving the First Oak Leaf Cluster to the Legion of Merit from Major General Dan C. Ogle, U.S.A.F. Surgeon General. The cere-

monies, held recently in General Ogle's Washington headquarters, were attended by Mrs. Kester and the senior staff of the Surgeon General.

General Kester was cited for his outstanding service to the United States in pioneering the development of a comprehensive and unique veterinary service as an integral part of the Air Force's worldwide medical service, and in broadening the use of Doctors of Veterinary Medicine in military research, preventive medicine and Air Force community health.

His approach in developing the Air Force Veterinary Service and in establishing the position of veterinary science on the military public health team has greatly broadened the concept and scope of military veterinary medicine. Trends and practices initiated by the Air Force have been followed by others in the medical and health fileds to the end that veterinary medicine and veterinary public health are better understood, more fully recognized, and more widely utilized in the betterment of human health and the welfare of the nation.

In retirement ceremonies following the award presentation, General Kester was cited in a personal communication from General Thomas D. White U.S.A.F. Chief of Staff for his splendid record of more than 24 years service.

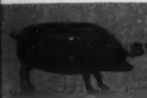
a true therapeutic restraint

Trilafon* veterinary

(pronounced Trĭl'-ah-fon) perphenazine

- controls the intractable animal without physical force
- achieves the desired degree of tranquilization without dulling normal responses

safe, effective dosage range for both large and small animals

animal	oral	intravenous	intramuscular
DOG	4 mg./10 lb. b. i. d.	5 mg./20 lb.	5 mg./20 lb.
 SWINE		10 mg./100 lb.	10 mg./100 lb.
ADULT BOVINE		75-125 mg.	100-150 mg.
CALVES & HEIFERS		adjust adult dosage according to body weight and degree of tranquilization desired.	

NOTE: Refer to Schering literature for complete information regarding dosage, side effects, precautions and contraindications.

PACKAGING: TRILAFON Tablets, 4 and 8 mg., bottles of 50 and 500.

TRILAFON Injection, 5 mg./cc., 10 cc. multiple-dose vial, *Small Animals* boxes of 1 and 6;
25 mg./cc., 30 cc. multiple-dose vial, *Large Animals* boxes of 1 and 6.

Schering

*T.M. V-TR-J-297

Forecast Influenza Epidemic

That an epidemic of influenza will sweep the United States from coast to coast this fall and winter is a "definite probability," according to releases from the office of the Surgeon General, Leroy E. Burney of the Public Health Service. There has already been widespread "seeding" of the infective virus and sporadic cases have been reported from widely separated areas. Should the disease occur in epidemic proportions, loss of man hours in vital service agencies is expected to seriously cripple these services. Business publications are warning that if Asian influenza strikes, disruption of community services, businesses, and government will suffer weeks of paralysis.

Work was commenced in this country on the preparation of a suitable vaccine shortly after identification of the virus in Hong Kong last spring, and before the first cases were reported in this country. At present six producers, including: American Cyanamid Co., Eli Lilly & Co., Merck, Sharp & Dohme, National Drug Co., Parke, Davis & Co., and Pitman-Moore Co. are working a "crash" program with two or three vaccine production shifts working seven days a week.

The vaccine is a chemically treated (killed) chick embryo culture product now being delivered in substantial quantities both as a monvalent (Asian) influenza vaccine and combined with types A and B virus for a polyvalent immunizing agent. Physicians will probably prefer and manufacturers will provide as early as possible the polyvalent product, although production problems will delay delivery of the latter.

Protection afforded is rated at 70% against field exposure having a duration of approximately one year.

Not enough vaccine will be ready prior to possible epidemic so that effort is being made to establish vaccination priorities.

▼ ▼ ▼

A new liquid feed supplement for cattle and sheep will be offered by U. S. Industrial Chemicals Co., under the patented product trademarked "Morea."

The supplement is a liquid mixture containing urea, ethanol, phosphoric acid, essential trace minerals, and molasses.

Keep Teat **OPEN** Keep it **MEDICATED**

Keep it ***MILKING***

INJURED TEATS, SCAB TEATS, STENOSIS, POST-OPERATIVELY

To maintain unrestricted milk flow and provide antiseptic protection is of first importance in the successful treatment of teat troubles. Dr. Naylor Dilators act both MEDICALLY and MECHANICALLY to provide broad spectrum germicidal activity and gentle, non-irritating support to traumatized sphincter and teat mucosa.

Contain Sulfathiazole — the self-contained anti-microbial medication in Dr. Naylor Dilators provides full time antiseptic activity in the entire streak canal. They do not depend upon packaging ointment for antiseptic or therapeutic properties. The medication is IN the Dilators and is released slowly IN the teat to combat infection, reduce inflammation and keep streak canal open to promote normal healing, natural milking. Positive retention in large or small teats!

WITH ANTIBIOTICS

Dr. Naylor Dilators are an ideal vehicle for additional local medication of your choice. To obtain the synergistic bactericidal action of Antibiotics with Sulfathiazole following teat surgery, saturate with your favorite udder infusion antibiotic.

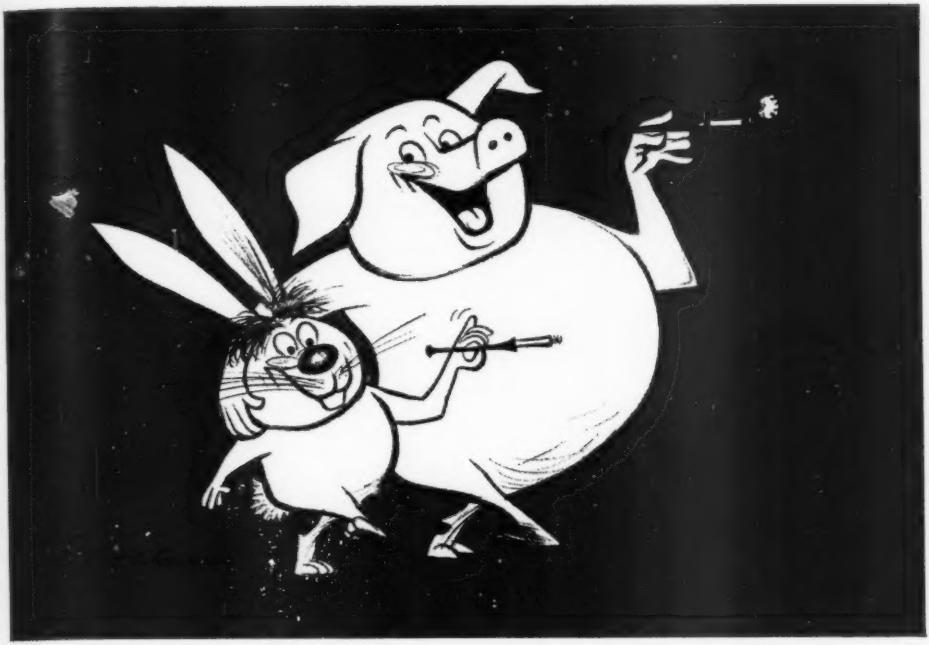
Dispensing Package
16 Dilators

Dr. Naylor's

MEDICATED

Large Pkg. 45 Dilators ***Teat Dilators***

H. W. NAYLOR CO., Manufacturing Chemists, **MORRIS, N.Y.**



NEW SAFE...SOLID IMMUNITY WITH

ROVINE* HOG CHOLERA VACCINE

(Modified live virus-rabbit origin-vacuum dried)

FOR USE WITH SERUM

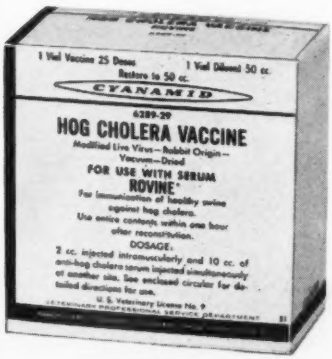
New ROVINE Hog Cholera Vaccine is a modified live virus produced by the adaption of hog cholera virus to rabbits.

This was followed by many serial passages in rabbits, bringing the virus to a degree of modification where it is no longer pathogenic but retains its ability to provide solid dependable immunity against hog cholera.

It is intended for use with anti-hog cholera serum. Administration is 2 cc. of ROVINE and 10 to 15 cc. of serum.

Sold only to veterinarians. For details please write VETERINARY PROFESSIONAL SERVICE DEPARTMENT, AMERICAN CYANAMID COMPANY, NEW YORK 20, N. Y.

*Trademark



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To the Profession it has served with undivided responsibility for so many years—BARD-PARKER has devoted its scientific knowledge and the inimitable skill of its craftsmen in developing the finest surgical blade possible . . . a blade that meets the demand of the Profession for quality and economy.

The satisfaction of knowing you have chosen the best is yours when you use B-P RIB-BACK blades.

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Danbury, Connecticut

UNIFORMLY SHARP
RIGID
STRONG

the 'only' RIB-BACK BLADE

MEETING CALENDAR

Southern Veterinary Medical Association. Annual Meeting. Roanoke Hotel, Roanoke, Va., Oct. 27-30, 1957. Dr. A. A. Husman, P. O. Box 91, Raleigh, N. C., secretary.

Omega Tau Sigma Annual International Convention. Alpha Chapter, School of Veterinary Medicine, University of Pennsylvania, Nov. 7-9, 1957. B. Joseph Tribolla, Oak Avenue, R.F.D. #2, Hilltop, New Jersey.

Midwest Small Animal Meeting and Regional A.A.H.A. Meeting. Hotel Burlington, Burlington, Ia., Nov. 13-14, 1957. Dr. J. Porter Coble, 2828 S. MacArthur Blvd., Springfield, Ill., secretary.

United States Livestock Sanitary Association. Sixty-first Annual Meeting. Chase-Park Plaza Hotel, St. Louis, Mo., Nov. 13-15, 1957. Dr. Ralph O. Hendershott, 33 Oak Lane, Trenton 8, N. J.

Arizona Veterinary Medical Association. Annual Meeting. Hiway House Hotel, Phoenix, Ariz., 2:00 p.m. Dec. 1 through 3rd.

University of Pennsylvania. Fifty-eighth Annual Conference of Veterinarians. School of Veterinary Medicine, University of Pennsylvania, Jan. 7-8, 1958. Dr. James Mark, program chairman.

New York State Veterinary College. Fiftieth Annual Conference for Veterinarians. Cornell University, Jan. 8-10, 1958. Dr. W. A. Hagan, Cornell University, Ithaca, N. Y., dean.

Oklahoma Veterinary Medical Association. Forty-third Annual Meeting. Hotel Lawtonian, Lawton, Okla., Jan. 9-10, 1958. Mrs. Larma Bennett, 2805 S. 51st St., Oklahoma City, Okla., executive secretary.

Kansas Veterinary Medical Association. Fifty-fourth Annual Convention. Hotel Broadview, Wichita, Kans., Jan. 12-14, 1958. Dr. K. Maynard Curts, 5236 Delmar Ave., Kansas City 3, Kans., secretary.

Iowa Veterinary Medical Association. Annual Meeting. Hotel Fort Des Moines, Des Moines, Ia., Jan. 14-16, 1958. Dr. F. B. Young, Waukee, Ia., secretary.

Indiana Veterinary Medical Association. Annual meeting. Hotel Severin, Indianapolis, Ind., Jan. 15-17, 1958. Dr. L. M. Borst, 3315 Shelby, Indianapolis, Ind., secretary.

Michigan State University. Thirty-fifth Annual Post Graduate Conference for Veterinarians. College of Veterinary Medicine, Michigan State University, East Lansing, Mich., Jan. 22-23, 1958. Dr. W. W. Armistead, dean.

Colorado State University. Nineteenth Annual Veterinary Conference. Glover Veterinary Hospital, College of Veterinary Medicine, Colorado State University, Fort Collins, Colo., Feb. 17-19, 1957. Lloyd C. Moss, Dept. of Medicine.

Illinois State Veterinary Medical Association. Seventy-sixth Annual Convention. LaSalle Hotel, Chicago, Feb. 17-19, 1958. C. B. Hostetler, 1385 Whitcomb Ave., Des Plaines, Ill., executive-secretary.

▼ ▼ ▼

The Ralston-Purina Company has announced that it has perfected and would begin marketing a high-fat pellet for broilers this fall. The new product will carry a guaranteed fat content of 8%, approximately twice as much as former production methods were able to pellet.

For the first time . . .
two *living*, modified viruses
are combined in

VIROVAX D-H*

[PATENT PENDING]

for simultaneous immunization
of dogs against

DISTEMPER and HEPATITIS

with a single injection

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CANINE DISTEMPER VACCINE
Modified Live Virus, Chick Embryo Origin
and INFECTIOUS CANINE HEPATITIS VACCINE
Modified Live Virus, Canine Tissue Culture Origin
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SOLD TO VETERINARIANS ONLY

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PEORIA, ILLINOIS

—DEATHS OF VETERINARIANS—

John R. Shikles, Dearborn, Mo., WES '06, June 29, 1957.

George F. Barton, Chilliwack, B. C., Canada, ONT '32, July 4, 1957.

Leo D. Bashore, Paulding, Ohio, CIN '15, June 5, 1957.

S. J. Collins, Reedsburg, Wisc., ONT '91, March 15, 1957.

Ralph L. Gangarosa, Gordon, Nebr., COR '40, July 3, 1957.

Eugene F. Pile, Lexington, Ky., KSC '16, died recently.

Gilbert S. Kirby, Warsaw, Mo., STJ '19, May 16, 1957.

Harvey H. Seely, Jerseyville, Ill., CVC '18, June 15, 1957.

Robert S. Tillie, Muscatine, Ia., ISC '16, April 26, 1957.

▾ ▾ ▾

The number and strains of bacteria that have developed resistance to penicillin is increasing rapidly, according to a report in *Nature* (Aug. 10). Antibiotic resistant microorganisms arrive by spontaneous mutation and occur as a new strain irregardless of whether the patient has ever received the drug.

▾ ▾ ▾

More than $4,000,000. worth of pigs now arrive dead at markets annually, according to USDA report.

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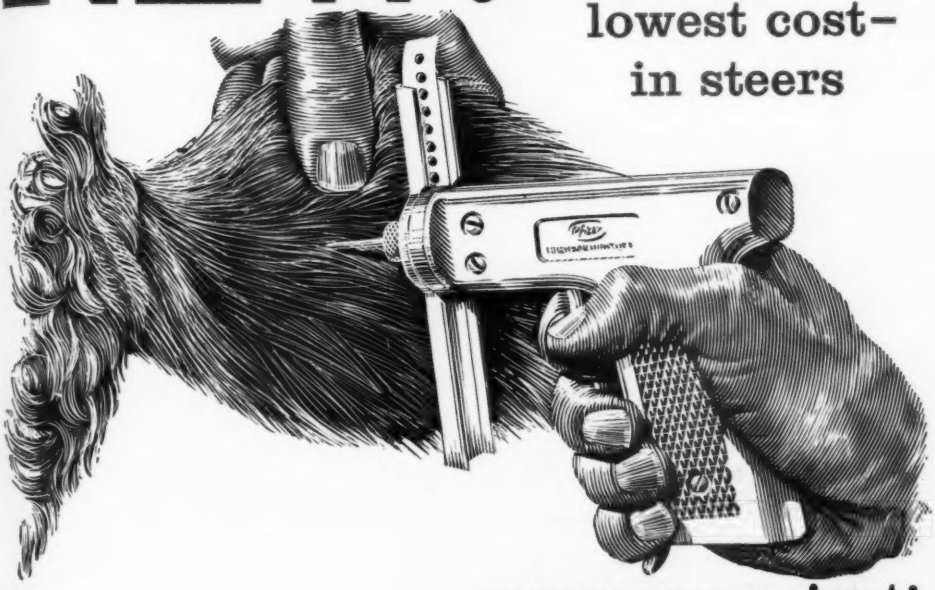

more convenient!
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A NEW STILBESTROL IMPLANT

A time saver in practice . . . indispensable for dispensing!

Pfizer's brand of stilbestrol pellets designed for administration by the Automatic Implant Gun—for *convenient, rapid,* and *low-cost* implanting of steers under *drylot* or *pasture* conditions.

Just *one* instrument, Pfizer's Automatic Implant Gun is all that is needed to implant the recommended 24 to 36 mg. dose of stilbestrol (two to three pellets). No nicking of the skin, no handling of extra instruments. A quick swab of the ear, easy insertion of the surgically sharpened needle under the skin, effortless pressure on the trigger and the animal is ready to be released. Special clips of pellets to allow treatment of three to five animals without reloading.

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- maximum daily weight gains with
- less feed consumption per unit gain at
- minimum cost.

STIMPLANTS Introductory Deal available from your Pfizer distributor: Clips of 10 pellets; each pellet contains 12 mg. of stilbestrol.

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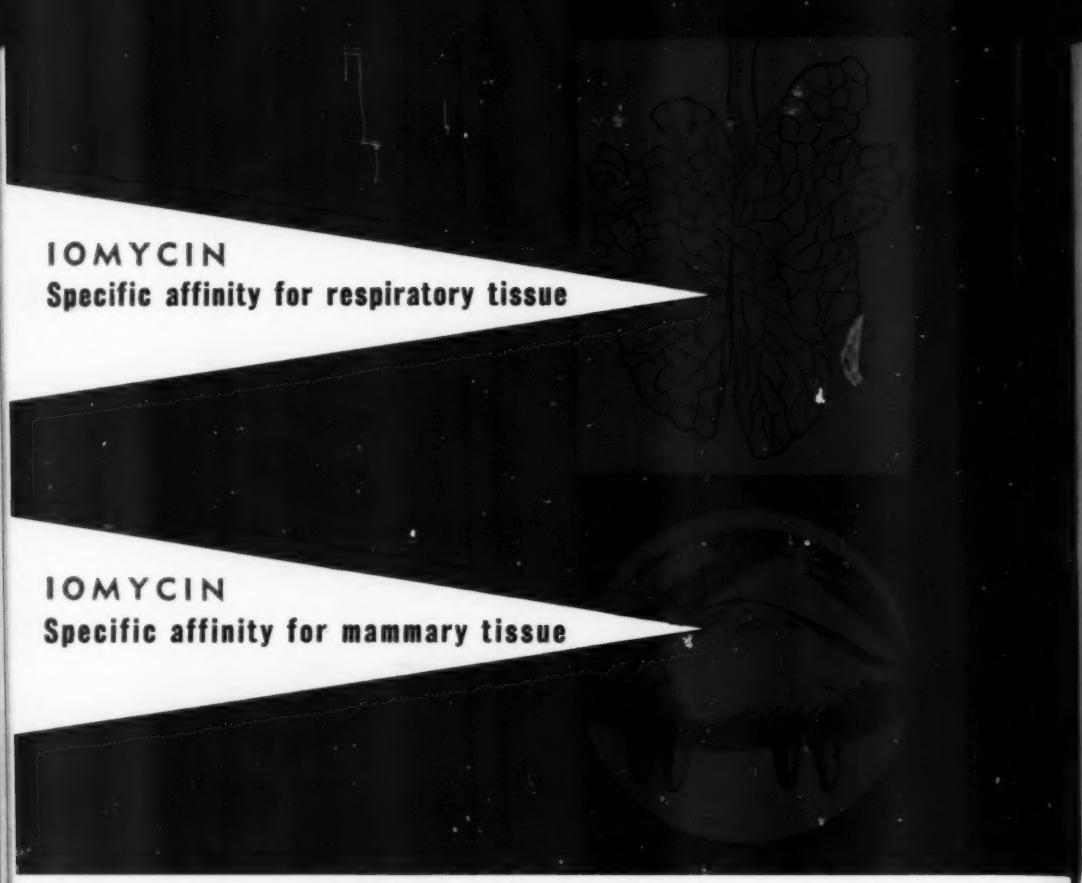
Division, Chas. Pfizer & Co., Inc.



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IOMYCIN is an entirely new *antibiotic* for intramuscular administration with unusual effectiveness in the treatment of mastitis and respiratory infections including: calf pneumonia, shipping fever, and feline and canine pulmonary infections.

IOMYCIN provides broad anti-bacterial spectrum *plus* specific and unusual affinity for respiratory and mammary tissues. Concentrations in these tissues are up to 5 times those resulting from an equal dose of procaine penicillin G.

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Diethylaminoethylesterpenicillin Ghydriodide; 2,000,000 units

Dihydrostreptomycin Sulfate (base), 2.5 grams

With sterile diluent for injection

Dosage Small animals: 0.5 to 1.5 cc, once daily, depending on size of animal and severity of infection. Continue administration 2 to 4 days.

Large animals: 1.0 cc for each 100 pounds body weight once daily for 2 to 4 days.

Supplied In: 10 cc Combination Powder-Diluent Univial

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DEPENDABLE, NON-GRIPING–

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FOR ALL
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UNIFORM CHEMICAL COMPOUND,
ISTIZIN IS RECOMMENDED
BECAUSE IT IS:

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- Economical
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Supplied in bottles of 1 pound and 5 pounds of powder and in ½ oz. boluses, boxes of 24.

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